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JOHNS HOPKINS HOSPITAL

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THE JOHNS HOPKINS HOSPITAL.

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THE DISSECTION AND LIBERATION OF THE SPHINCTER ANI MUSCLE FOLLOWED BY ITS DIRECT SUTURE IN CASES OF COMPLETE TEAR OF THE PERINEUM, WITH A SPLINTING SUTURE PASSING BETWEEN THE OUTER AND INNER MARGINS OF THE MUSCLE.

By H. A. Kelly, M. D., *Gynecologist-in-Chief, The Johns Hopkins Hospital.*

Although great progress has been made in gynecological plastic surgery within the past twenty years, there have been few or no changes in the treatment of complete perineal tears, that is, those which extend through the external sphincter ani.

The common symptom of a complete tear of the perineum is the lack of a control over the functions of the bowel, characterized by the involuntary escape of feces and gases. These sequelæ, however, are not invariably present in the same degree in all cases, and there is a diversity among them varying all the way from the entire loss of function on the one hand to perfect control on the other.

Some surgeons, reasoning upon supposedly physiological grounds, have gone so far as to assert that it is impossible for a woman with a divided sphincter to exercise any control whatever over the bowel function; I know, however, from repeated clinical evidences that perfect function may sometimes persist; it becomes therefore necessary to discover some satisfactory explanation of the facts rather than to deny them.

I would divide the cases of complete tear, to be investigated from this standpoint, into two groups. First, those in which the tear barely extends through the sphincter and goes no further, and, second, those in which the sphincter ends are separated by a well-defined interval of a centimeter or more.

In the first of these groups, where the muscle is only just divided and the ends lie close together, the cicatrization which follows the injury is a conservative effort on the part of nature, and soon results in the approximation of the ends of the muscle, knitting them firmly together, with only a plug of scar tissue between. In this event the muscle is no longer, in a true sense, a sphincter, as it cannot contract from all directions towards a central point, but is compelled henceforth, by the break on one side and the interposition of a plug of unyielding connective tissue, to contract up to the scar as a more or less fixed point, and this it does with greater or less efficiency. This peculiar effect produced upon the sphincter

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by the interpolation of a mass of scar tissue was point[illegible] many years ago by Hildebrandt.

The second group relates to those cases in which the [illegible]ter ends are not bound together; I have at present un[illegible] care a patient with a complete rupture of the perineu[illegible] deep, perfectly marked sphincter pits, separated by the [illegible]rc breadth of the anal [illegible]ifice, with a relaxed everted vagina[illegible]let and a uterus in des[illegible] retroversion, and yet she has ab[illegible] lute control over [illegible] and is never disturbed by involuntary escape of gase[illegible] is the explanation of this fact.

A careful physical examination shows that the patient has perfect voluntary control over the internal sphincter muscle, extending from the external sphincter about 2 cm. upwards.

The tonic contraction of the internal sphincter and its response to a voluntary effort can be most readily tested *in propriâ personâ*. If the tip of the finger is well oiled while sitting in a warm bath and inserted about an inch into the bowel while slightly bearing down to relax the sphincter, then, upon causing a voluntary contraction, a prompt response on the part of the internal sphincter will be noticed. When not voluntarily relaxed, the internal sphincter is in a state of tonic contraction guarding the orifice, while the external sphincter is not always contracted.

I believe, therefore, from repeated clinical observations that the tonic control exercised over the bowel functions resides rather in the internal sphincter ani than in the external, and that the external sphincter muscle is a provision against an emergency and is intended to form a temporary, powerful supplement to the internal sphincter.

The external sphincter is of further use in the act of defecation, in breaking the fecal column at intervals, so tending to prevent prolapsus recti by creating a pause in the act and allowing time for more material to pass down into the rectum before the renewal of the straining.

This physiological fact explains the reason why, when the external sphincter ends lie close together and the internal sphincter is therefore uninjured, continence is always preserved.

I would add, too, to this category of manifest sphincter injuries, a much larger group of cases in which, owing to the fact that control over the bowels is retained, as well as owing to the natural, uninjured appearance of the anus, suspicion is disarmed, and the surgeon, even when he is brought into such close contact as is involved in the performance of a perineal operation, fails to recognize the fact that the sphincter ends are divided. I cannot sufficiently emphasize the importance of this observation, and therefore reiterate my conviction that many women have torn sphincters which are never discovered.

When the ends of the external sphincter muscle are separated by any considerable interval in a recent tear, the [illegible] internal sphincter is also torn, and, the wider the separati[illegible] of the external sphincter ends, the greater the tear into the [illegible]owel and therefore of the internal sphincter above. What is t[illegible] of the recent injury is true *a fortiori* several months later, w[illegible] a wide tear is drawn down to a narrow line and an interva[illegible] of 1 cm. between the pits may represent a rupture 3 cm. in d[illegible]pth. It is therefore to this tear of the internal sphincter tha[illegible] the loss of control over the bowel functions is due.

Operation.—The prevailing operation in this count the Emmet, which I need not describe in detail as it is sc known. The operations practiced in Europe for the most are of a similar nature, or flap-splitting or Hegar's me The important principle in the Emmet procedure consi the application of a series of sutures, to an area thorou denuded, first closing the bowel, then radiating out fron bowel, over the skin and onto the vaginal surfaces. En further lays great stress upon a tension suture entering emerging at points outside of and well behind the exte sphincter ends and traversing the septum, for the purpo supporting and keeping [illegible] two thirds of the sphincter together. Dr. Emmet told me on one occasion that devising of this suture cost him more thought than anything he had done in gynecology.

Although this operation, as well as the others menti when well carried out, succeeds admirably in many insta it still leaves much to be desired in that there does rem residuum of failures, and a considerably larger percenta cases in which the function is so imperfect at first that w obliged to wait [illegible]r months for the patient to ga satisfactory cont[illegible] [illegible] in this latter group i are women who [illegible] that when their bowels bec loose they alw[illegible] their clothes more or less fo while they are also apt to be uncertain about the [illegible] of gases.

In order to meet the various objections to the opera as practiced at present, I have devised several procedure upon the physiological principles dwelt upon above; the important point is the dissection and liberation of both end the sphincter muscle, after which they are sutured toget with buried cat-gut sutures, end against end.

I can perhaps best emphasize the importance I wish to g this step by citing the first case in which I was led to oper in such a way.

Case I.—The patient was brought to me in Dec., 1897, by Dr. J. Sexton, of Raleigh, N. C. She had had six previous operations p formed for complete tear of the recto-vaginal septum, and up inspecting the parts I found perfect union throughout, a patholo cally small well-closed anus, and a far better result in the exter appearance than is often secured in cases which are deemed su cessful. In spite of appearances, however, she had no control ov the function of the bowel, and the gases escaped audibly at all time and formed movements were discharged at once without t slightest ability on her part to restrain them (Fig. 1).

I was disinclined from my examination to do anything furth to this patient, after all she had passed through, doubting wheth I could improve her condition, but through Dr. Sexton's kin insistence I felt at last forced to make at least an earnest effort to better her state. So I operated Dec. 8, 1897, determined to make a clean dissection of the external sphincter, even, if necessary, going so far as to lay the entire muscle bare, so as to make sure of bringing its ends into apposition, and leaving the end of the bowel encircled by a good muscular ring, if one could be found in the neighborhood.

I began the operation by making a semilunar incision with its convexity directed towards the symphysis, half way round the anal orifice and about 1 cm. from the anal margin (Fig. 1). As the dissection through the scar tissue was carried into the perineum, the edges of the incision were drawn in opposite directions, exposing a wide crescentic area. I found now that the sphincter could be beauti-

fully demonstrated anatomically, and that the right end lay nearly in the normal position, but fixed in the median scar, while the left end lay at least 2½ cm. distant from the right end, and was attached to the tuberosity of the ischium (Fig. 2). After laying bare and freeing 2 cm. of each of the ends, I then trimmed off the scar tissue so as to expose fresh red muscular bundles, which I then united with three interrupted buried cat-gut sutures, simply transfixing the sphincter muscle 5 or 6 mm. from the cut ends. Two buried sutures were also used in the septum in the deeper fat layer of the wound, and the skin wound was finally closed with fine silk sutures (Fig. 3). The result was a perfect union and greatly improved control of the bowel from the first. I examined the patient again two months later, and passing a finger a short distance into the rectum and grasping the sphincter between finger tip and thumb could distinctly isolate it on all sides, and on telling her to contract the muscle I could feel that it was perfect throughout and under complete control.

I do not know of any other instance in which with an apparently well-formed anal orifice the sphincter muscle has been laid bare and the separated ends freed from their attachments and then joined by buried sutures.

Following the initiative of this case, I at once incorporated the dissection, isolation and separate suture of the sphincter muscle as an essential part of the technique of all my operations for complete tears, intending in this way to insure the bringing of the sphincter into the field as well as the exact union of its parts, end to end.

CASE II.—The next case was one of the classical sort, a secondary operation for complete tear where the parts had well cicatrized.

She was operated upon towards the end of February, 1898. She had had a complete tear of the perineum in consequence of a forceps labor conducted by myself in the preceding December; the immediate suture failed, and since that time she had had no control whatever over the bowel function. In place of the perineum there was a boat-shaped cicatrix extending from two lateral prominences marking the former position of the fourchette, extending back to the anus. The recently cicatrized tissue fairly marked out the extent of the original tear in somewhat diminished form. I proceeded by denuding the vaginal sulci and the lateral surfaces as usual. I then exposed the sphincter ends by turning down a triangular flap of uninjured skin lying in front of the anus (see Fig. 4), catching the ends in their pits one at a time, pulling them up and out a little, and snipping with blunt-pointed scissors on all sides of the eminence until each sphincter muscle stood dissected out with perfect distinctness about 2 cm. beyond the surrounding tissue. On lifting the ends up the pull on the posterior part of the sphincter could be distinctly felt with the thumb and forefinger grasping the margin of the anus. The exposed ends were then denuded of the film of scar tissue covering them and brought evenly together with interrupted cat-gut sutures; the flap which was turned down over the bowel during the dissection was then brought up over the sphincter, and the rest of the wound closed as usual. The result was a perfect control over the function of the bowel from the very first, leaving nothing to be red in respect to function, and the patient has now, a year r, absolutely normal control.

ASE III.—In my third case I was obliged to follow a somewhat dif- ent procedure, as the sphincter pits were not well enough marked r me to be sure of their identity. After making the usual denu- ation I then made two incisions parallel to the sides of the anus nd extending downwards from the denuded area about 1½ cm. on ither side (see Fig. 5). On pulling apart the tissues and dissecting nwards, the sphincter muscle was then clearly exposed, freed from ts bed, and the ends cut off (Fig. 6). The rectal part of the tear was ow closed by interrupted sutures applied on the rectal side down the sphincter area, and a short distance out onto the skin surface (Fig. 7). The sphincter ends were then denuded and brought together with buried interrupted cat-gut sutures passed through them, after which the rest of the wound was united as usual (Fig. 8), and the para-rectal incisions carefully closed with interrupted cat-gut sutures.

Since then the following cases given in abstract have been operated upon in my clinic by Drs. Russell, Ramsay and myself.

CASE IV.—B. D., married, age 23, white.

Diagnosis.—Complete tear of perineum.

Operation.—Restoration of ruptured recto-vaginal septum.

The patient has been married five years and has had two children and one miscarriage. The first labor was difficult and instrumental, at the second the child was still-born, while one month previous to admission, the miscarriage had taken place at four months.

Ever since the birth of the first child, three years ago, she has had a descensus of the womb, with bearing-down pains in the abdomen, pain in the back and headache, all of which symptoms have been worse during the past 3 months, the prolapse now being marked. The bowels move regularly every day.

Examination under ether showed: Extensive tear of recto-vaginal septum, through sphincter ani and up left sulcus, the tear apparently extending one inch into rectum.

Operation by Dr. Kelly, March 12, 1898. The usual Emmet denudation was made, and, in addition, the sphincter ends were dissected and pulled out on either side, 3 cm. on right and 2½ cm. on left, clear of all surrounding tissue. About 3 mm. of the ends were cut off to remove the white scar tissue and to present an even muscular surface; the ends were then sutured directly together with 4 cat-gut sutures and dropped and buried.

The septum was first united down to the sphincter, after which the sphincter was united, and then the remaining portion of bowel and finally the vagina and perineum. A silkworm-gut tension suture was inserted behind the sphincter ends but not so far posteriorly as usual. Duration of operation, 35 minutes.

Convalescence was uninterrupted; the healing was *per primam* and the result perfect; the patient had perfect control of the bowel from the very first. Maximum temperature 98.8° (2d day). Discharged well April 2, 1898.

CASE V.—F. G., married, age 26, white.

Diagnosis.—Retroflexio uteri; tear of the perineum, extending through the sphincter ani.

Operation.—Suspensio uteri; restoration of ruptured recto-vaginal septum.

The patient on admission complained of pain in the bladder and misery in the back. She had been married seven years; had had three children and no miscarriages. All three labors were difficult, the first two were instrumental, and in both these the outlet was lacerated with no attempt at subsequent repair. The last child was born two years ago.

The bowels were extremely constipated; she had hardly any control over them, especially as regards flatus.

Examination under ether showed: Outlet greatly relaxed; complete tear of perineum, extending through into bowel, the sphincter pits being distinct on either side; uterus in retroflexion.

Operation by Dr. Kelly, April 13, 1898.—Denudation in sulci and on lateral walls of vagina as usual, extending down to rectum and laterally to sphincter pits; ends of sphincter dissected out and caught with forceps; rectum brought together in the usual way by interrupted cat-gut sutures, tied on the rectal side; ends of sphincter muscle freshened and brought together with 4 cat-gut sutures; a deep silkworm-gut tension suture was also inserted behind the sphincter ends; rest of closure in usual way. Uterus suspended in usual way. Time of complete operation, 75 minutes.

The *convalescence* was marked by a partial breaking down of the perineal incision, with some suppuration, but the perineum was

well lifted up, and introduction of finger into rectum showed good sphincter action, except anteriorly, while the patient seemed to have good control over her bowels. The maximum temperature was 100° (on the 7th day). The patient was discharged May 10, 1898.

Subsequent note, Aug. 27, 1898.—Result of perineal operation is fair; some bulging of anterior vaginal wall, and pressure upon it and upon uterus causes discomfort. Sphincter ani has apparently its full power. Since leaving the Hospital the patient has improved in general health and is free from her old trouble, except some pain in the back and painful micturition.

Cystoscopic examination showed that the bladder was inflamed and infected, especially about the region of the trigonum, while the urine showed a great number of pus cells and a small amount of albumen.

Case VI.—L. E., married, age 30, white.

Diagnosis.—Complete perineal tear.

Operation.—Restoration of ruptured recto-vaginal septum.

Marital history.—Married four years, two children and two miscarriages. The first labor, three years ago, very difficult, although not instrumental; the patient was lacerated, and the laceration was repaired, but not successfully; the second labor, one year ago, was not difficult.

Since birth of first child, she has had prolapse of uterus after standing for some time, the uterus returning to its place on lying down. Has absolutely no control over her bowels and but little over urination. Feels as if bladder prolapsed with the uterus. The patient suffers with dragging pain in the back and loins. All these symptoms have been worse since the birth of her last child.

Examination.—Complete tear through perineum and sphincter ani muscle, about one inch of the bowel being seen. Uterus in anteposition, low down in pelvis. Outlet greatly relaxed.

Operation by Dr. Russell, April 28, 1898.—Tear extended 3½ cm. beyond sphincter into bowel. Sphincter ani ends were dissected out free; the mucous membrane was united above the sphincter by interrupted cat-gut sutures; the ends of the sphincter were then united directly with 4 cat-gut sutures, 1 tension silkworm-gut suture going from side to side through the skin and the septum. The outlet was then restored in the usual manner. Time of operation, 50 minutes.

The *convalescence* was uninterrupted; the bowels were well moved on the fourth day; the wound healed perfectly; the sphincter ani has good power, and the patient has perfect control of her bowels.

The patient's maximum temperature was 100° (2d and 7th days). The patient was discharged May 20, 1898.

Case VII.—M. B., age 32, married, white.

Diagnosis.—Large retroflexed uterus with descensus; lacerated cervix; complete tear of vaginal outlet with concealed tear of sphincter ani.

Operation.—Trachelorrhaphy; restoration of ruptured recto-vaginal septum; suspension of uterus.

Married 13 years; has had three children and one miscarriage; all three labors were prolonged and very difficult, and the perineum was badly torn each time, the worst tear being at the last delivery, three years ago. No one of the labors was instrumental.

Since the birth of her second child, six years ago, the patient has had dragging and bearing-down pains in the lower abdomen, aggravated by walking or climbing, with progressively increasing loss of strength and loss of weight. Micturition has been increased in frequency and is occasionally painful.

The bowels are generally regular, but, since the birth of the last child, she has had difficulty in controlling the fecal movements whenever the bowels are loose.

Examination.—Uterus is enlarged and retroflexed. The vaginal outlet is so relaxed that the cervix is visible. A tear is seen extending up the median line into the rectum about two cm. in length. Slight lateral indentations indicate the possible position of the sphincter ends and this is verified by palpation or stimulation; the sphincter retracts on all sides except in front. The lips of the cervix are everted and congested.

Operation by Dr. Kelly, June 18, 1898.

Dilatation and curettage with the removal of abundant endometrial detritus. The lacerated cervix was repaired next, and then the vaginal outlet, including the sphincter ends; after the denudation of the wound area the sphincter ends were dissected and drawn out to the extent of 1 cm. Some scar tissue was then cut off the ends to make them square and fresh. The rectal side of the tear was then closed with six cat-gut sutures down to the sphincter ends; the ends were then pulled out and held so, while *a silkworm-gut suture was passed through the skin, through one sphincter end across the septum and out through the opposite sphincter end and through the skin again.* The sphincter ends were then accurately approximated by three cat-gut sutures. The rest of the operation was performed in the usual way.

The uterus was also suspended through an abdominal incision. Time of complete operation, 55 minutes.

The *convalescence* was uninterrupted; the healing was perfect; the vaginal outlet was well lifted up, with the cervix in good position as well as the uterus and the patient had perfect control of her bowels. Maximum temperature 99.8° (third day). Patient was discharged July 16, 1898.

Case VIII.—E. N., married, age 47, white.

Diagnosis.—Multiple cervical polypi. Polyp of posterior vaginal wall. Rupture of recto-vaginal septum.

Operation.—Removal of polypi; amputation of cervix; repair of perineal tear.

Marital history.—Married at 18, seven children (oldest 25 years, youngest 5 years). Always had normal labors and was never attended by a doctor.

Menstrual history.—For the past six months has had frequent hemorrhages until a few (5 to 6) weeks ago, since then no flow at all. Associated with the hemorrhages were pains in legs and pelvic regions, which have continued up to the present time, occasionally associated with "colicky" pains in left hypochondrium. Bowels were usually regular up to the time of the hemorrhages, since which time they have been constipated. Micturition has increased somewhat in frequency of late. Urine is negative.

Examination under ether showed: Outlet gaping; complete tear of recto-vaginal septum, sphincter pits being definitely marked on both sides, with a bridge of scar tissue holding the ends of the muscles together. Several cervical polypi; one polyp of vagina; uterus enlarged, but in anteposition.

Operation by Dr. Ramsay, June 19, 1898.—Removal of vaginal polyp; amputation of cervix with its attached polypi; the denudation of the complete tear was made in the usual way to the sphincter pits; the ends of the sphincter muscle were caught, drawn out and dissected free. Cat-gut was used to draw together the bowel above the sphincter; the sphincter ends were then brought together with three cat-gut sutures, with a silkworm-gut suture *through the muscle* and the septum to relieve tension. The closure of the rest of the wound was performed in the usual way. Time of entire operation, 90 minutes.

The *convalescence* was uninterrupted; the healing was per primam, while by rectal examination the sphincter ani muscle could be felt contracting all around. The patient complained slightly of some pain in the left inguinal region which was relieved by enemata of starch water and fluid extract of Hamamelis. The maximum temperature was 100° (on 2d day). Patient was discharged well on July 20, 1898.

Case IX.—Mrs. C. H., married, age 36, white.

Diagnosis.—Complete perineal tear; relaxed vaginal outlet.

Operation.—Restoration of ruptured recto-vaginal septum.

The patient has been married 16 months and has had one child,

born 15 weeks ago ; she was in labor three days, and the delivery was finally completed by instrumental interference, during which she was badly torn, both at outlet and cervix ; an unsuccessful attempt was made to repair the septum. Since the childbirth she has had severe pains in back and pelvis, with partial loss of control of the bowels, especially marked when the movements are loose. As a rule however the bowels are constipated.

Examination under ether showed: Outlet much relaxed, with a tear through the recto-vaginal septum. Sphincter pits are easily seen, the one on the left side being pulled 2½ cm. from the position in which it is usually seen (apparently by the transversus perinei muscle). Uterus in anteposition and freely movable.

Operation by Dr. Kelly, June 27, 1898.—On palpation sphincter ani muscle felt easily posteriorly and laterally but not anteriorly. A verticle cut 1 to 1.5 cm. long exposed the sphincter ends. The sphincter was dissected out, the ends pulled out to the extent of 2 cm. and splinted by *a silkworm-gut suture passed through the muscle and up through the septum* and left untied for the present. The vaginal wound was closed, doing away with the relaxation; the rectal tear was closed and then the silkworm-gut suture was tied and the sphincter ends united by four cat-gut sutures, with two silkworm-gut sutures to perineum above and the rest cat-gut, making good closure throughout. Time of operation, 38 minutes.

The *convalescence* was uneventful until July 10, when, on the removal of the external stitches, although the wound had apparently healed well, the sphincter held well, and the patient apparently had perfect control of the rectum, it was found that there was a recto-vaginal fistula, the fistulous opening being around the internal vaginal suture on the left side. On the removal of this a good deal of soft fecal matter oozed through the opening, through which a sound 3 mm. in diameter could be passed.

This of course necessitated a *second* operation, which was performed on July 14, 1898. The sphincter was found to have held well ; the fistula was just within the vagina and opened into the rectum about 1½ cm. within the anus. The sphincter was first dilated, and through the sphincter the rectal opening of the fistula was found ; its edges were now pared and freshened on the rectal side ; the vaginal side was then freshened in the same way. The rectal mucosa was closed with fine silkworm-gut sutures, with the knots turned into the bowel, and the vaginal opening was closed in the same way, with the knots toward the vagina. A rectal plug was then inserted.

The *convalescence* from this second operation was uneventful, except for the difficulty in moving the patient's bowels. Perfect healing took place, and the fistula was obliterated. The maximum temperature was 101° (sixth day after first operation). The patient was discharged on Aug. 2, 1898.

The patient was readmitted Sept. 9, 1898. She complained of pain at stool, which had been present ever since her discharge from the Hospital, with discharge of liquid material at times ; the sinus seeming to heal for a day or two and then at stool to break down again.

Examination under ether showed: The sphincter ani muscle forms a *complete* ring around the anus, with normal radiating lines surrounding the orifice ; while a sinus, slightly to the left of the median line in the perineum, opens just within the sphincter muscle ; extending also 1½ cm. up in the recto-vaginal septum.

Operation by Dr. Russell, Sept. 14, 1898.—The sinus and the indurated tissue about it were dissected out ; the opening in the rectum was enlarged by paring the edges and was then closed by five cat-gut sutures, passed on the rectal side. A few buried cat-gut sutures were also introduced on the perineal side. The perineal incision was then closed with interrupted silkworm-gut and cat-gut sutures. The *convalescence* was uninterrupted, the healing was perfect, the temperature never rose above 99°, and closure was complete. The patient was discharged Oct. 7, 1898.

CASE X.—C. C., married, aged 38, white.

Diagnosis.—Relaxed vaginal outlet. Rupture of sphincter ani muscle.

Operation.—Dissection and direct union of the ends of the sphincter ani. Resection of the relaxed outlet. Curettage of cervix.

Marital History.—Has been married 15 years. Has had four children, no miscarriages. All the labors were extremely protracted and difficult. The first and fourth labors were instrumental; the third child was still-born. After the birth of the first child she had convulsions. At her last labor she was badly torn, the tear extending to the anus, but no attempt at repair was made. Phlegmasia alba dolens complicated her last puerperium. The first child is fourteen years old, the last (if living) would be two. The laceration mentioned above has never troubled her. The bowels are perfectly regular and under control, while there is an increase in the frequency of micturition.

Examination under ether showed : Tear of perineum through sphincter muscle and 1 cm. into the bowels above ; the ends of the muscle widely separated and connected by a narrow band of scar tissue ; a slight bilateral laceration of cervix ; uterus of normal size and in anteposition.

Operation by Dr. Russell, August 1, 1898. The operation was performed in two steps.

(1) A semilunar incision was made at anal orifice at junction of skin and mucosa, the flaps were dissected back and the ends of the sphincter ani muscle exposed ; the mucous membrane was united by cat-gut sutures, and then the muscle ends were drawn together and sutured with five cat-gut sutures. The primary incision was then united from side to side.

(2) The relaxed vaginal outlet was then resected in the usual way. Time of entire operation, 50 minutes.

The *convalescence* was only interrupted by the inability of the patient to void her urine and the consequent necessity of catheterization for the first week, followed by a mild cystitis, relieved by vesical irrigations.

The maximum temperature was 100° (on the second and eighth days). The wound in the rectum healed per primam ; perfect union of the sphincter muscle was obtained, with perfect control of the rectum. There was a slight infection of one of the vaginal stitches. The patient was discharged well, September 1, 1898.

CASE XI.—Mrs. C. W., married, aged 43, white. Private hospital.

Diagnosis.—Complete tear of the perineum.

Operation.—Repair of the complete tear. Dissection and direct suture of the sphincter ani.

The patient has been married 23 years and has had six children, the youngest three and a half years old, and one miscarriage in 1890.

She was badly lacerated at her first confinement, when the delivery was instrumental (22 years ago); this was repaired by Dr. Helmuth, in 1891, and the perineum was ruptured again at the birth of her last child, three and a half years ago.

She complains of general poor health, frequent attacks of diarrhœa, and especially of an escape of gas from the vagina ; she has also noticed fecal matter in the vagina ; and often has great difficulty and sometimes entire inability to control the movements of the bowel.

Examination showed : The vaginal outlet torn through and the sphincter ends widely separated ; the perineum boat-shaped, with much scar tissue between the vaginal and rectal openings, and the injury to the sphincter ends might easily be overlooked ; the sphincter ends marked by pits two cm. apart.

Operation by Dr. Kelly, November 22, 1898. Denudation as usual, removing scar tissue over sphincter ends and freshening the torn septum, extending up both right and left vaginal sulci. In including the sphincter ends, *the incisions marking out the area for denudation were made differently from the rule by*

cutting about three mm. away from the pits. This was done so as to give the sphincter a wider berth, so that when the sphincter ends were united by buried sutures they would not lie so close to the skin surface as they would if the incision was made close to the ends. Both sphincter ends were caught with forceps, pulled up and dissected out with a pair of blunt scissors until they appeared about one and a half cm. long above the surface. The glazed white ends were then cut off, and the rest of the denudation completed, and the bowel above freed from the recto-vaginal septum.

The rectal rent was then closed by fine interrupted silk sutures passed on the rectal side, *entering and emerging on the mucosa about one cm. from the margin of the cut.*

After closing the rectal rent, *the sphincter was united by two cat-gut sutures* and *splinted by silkworm-gut sutures entered about one and a half cm. back of the edge of the cut in the anal margin, and carried up through the septum, piercing the sphincter both on entering and emerging.* Another suture was passed well behind this first one, up through the septum outside the sphincter as recommended by Emmet.

The skin margin was very carefully closed up over the sphincter, and the rest of the wound in vagina and perineum united as usual, *extreme care being taken not to leave any dead spaces.* The intelligent patient had perfect control over the sphincter from the first, and at once recognized the great difference in her condition. She made a prompt recovery and returned home entirely well.

The one remarkable and constant fact specially noted after each of these operations was the immediate sense of restored power which was discovered by the patient as soon as she was well over the effects of the anesthesia; there was a sense of natural control over the function of the bowel which had been absent since the injurious confinement.

In conning the literature of this subject I have discovered several interesting references which have a direct bearing upon the method described. In the first place Dr. R. L. Dickinson,* has pointed out in an admirably clear paper devoted to the study of recent injuries to the sphincter ani, the important fact that the rupture of the muscles crossing the pelvic floor, in common with the external sphincter, is never median. The tear takes the direction of least resistance and avoids the aponeurotic web where the structures interlace in the middle line, breaking through laterally and severing the transverse perineal muscles and the sphincter well to one side. Out of sixteen cases ten were on the right, six on the left side, while another involved both sides of the sphincter. A close examination will always reveal an asymmetry, and not infrequently one end of the sphincter is found hanging out free on one side of the rupture, while the opposite side presents a deep pit from which it has been torn out. At the bottom of this pit is the other sphincter end. With the changes which take place during the period of cicatrization and contraction, well delineated by Kuestner and Leopold, this asymmetry is reduced to a minimum so that there finally remains but a slight obliquity in the level of the sphincter ends as a small index of a large difference earlier in the history of the case.

In these recent tears Dr. Dickinson with good surgical judgment used buried cat-gut sutures to bring the sphincter ends together; he says: "Two buried cat-gut sutures carried through the free hanging end of the muscle and then down into the pit to catch the hidden end, draw the parts into accurate apposition. The rest of the injury is then repaired as usual."

Sawaisky in an inaugural dissertation published in St. Petersburg, 1895, describes a method of treatment employed in Prof. Lebedeff's clinic in six cases of complete rupture. The recto-vaginal septum was first split as in performing a flap operation, and then after extending the wound sufficiently up onto the vulva the ends of the sphincter were caught and united with an interrupted suture, after which the major part of the wound was closed with a continuous cat-gut suture, and the closure was completed with four deep and two superficial sutures.*

In an article by Leopold and Wehle †, a method of uniting the sphincter is described by which two or three sutures are passed through the skin close to the sphincter, brought out in the sphincter pit and re-entered on the sphincter on the opposite side to reappear on the skin surface at a point corresponding to the point of entrance. By this means the suture ends are approximated with far greater accuracy and with a degree of certainty unknown in the old operation; this is practically the same method I have been practising myself for a number of years past.

Dr. George E. Shoemaker, in a personal letter received January 14th, 1899, states that he operated upon a tear of the sphincter ani muscle in June, 1893, which was referred to briefly in the *Medical News* of September 22d, 1894. Two previous operations, both unsuccessful, had been performed on the patient for the same trouble which had originated in 1891. Dr. Shoemaker's operation was begun by making a curved incision from over one sphincter end across to the other. The sphincter muscle ends were then dissected out and clearly defined, after which they were caught up by a strong cat-gut suture which included only the two sphincter ends. The rectal wall was closed in the usual way and the Emmet intravaginal denudation completed, two reinforcing worm-gut sutures being passed through the sphincter, each beginning far out on the skin at the side and ending at a point opposite.

The operation was entirely successful and the patient secured perfect control of the bowel.

Since this operation Dr. Shoemaker states that he has used this method repeatedly with entire satisfact

In a brief but suggestive paper Dr. R. G. L the direct suture of the sphincter ends by cat-gut suture passed after the fashion of a ten sphincter ends are hooked up and drawn forward and freshened either by cutting off a small portion with the scissors or by fraying the ends well with a knife, as already advised by previous operators who have insisted on freshening the sphincter ends as essential to secure good union; two cat-gut sutures are then applied one on each side of the sphincter muscle, and two more on the opposite side; when the opposed sutures are tied the sphincter ends are approximated. Dr. J. M. Baldy skilfully carried out Dr. LeConte's suggestion with remarkable success upon a patient who had been twice previously operated upon with an unsuccessful result each time.

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* Amer. Gyn. and Obst. Jour., May, 1895.

* See reference in Frommel's Jahresbericht, Vol. 7, p. 202.

† Geburtsh. u. Gynaek., Bd. 2, Leipzig, 1895, p. 307.

‡ Amer. Jour. of Obst., June, 1895.



Fig. 1.—Showing the natural appearance of orifice after six attempts to restore the sphincter and secure control over the bowel function. The dotted line shows where the incision was made to expose the sphincter ends. A and B are pulled apart as shown in the next figure.



Fig. 2.—Shows the sphincter ends as they were found on pulling flap A up and flap B down. The right end lay near the median line and the left displaced attached close to the tuberosity of the ischium. One of the catgut sutures in place ready to bring sphincter ends together.



Fig. 3.—Appearance after the union of the sphincter ends and the closure of the skin wound, with interrupted silk sutures.



Fig. 4.—Showing skin flap held down and sphincter ends united by 3 interrupted catgut sutures. This was a case of deep injury of the sphincter without tear of the skin over the anus and without a tear into the lumen of the bowel.

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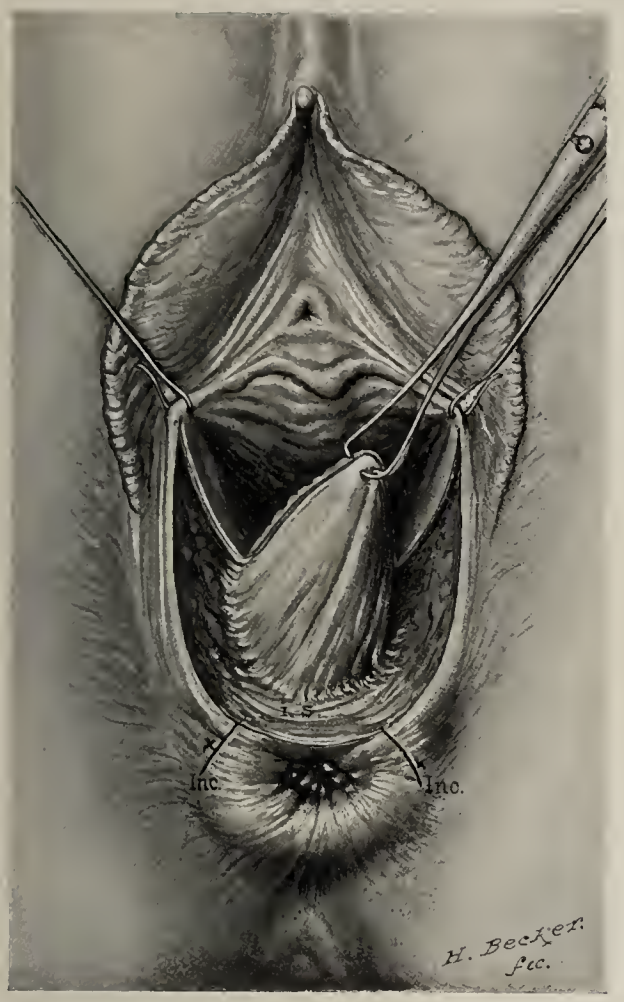


FIG. 5.—The denudation on vaginal and perineal surfaees. The tongne of tissue in the middle lifted np and dissected loose from the internal sphincter (i. s.). The denudation does not, however, expose the external sphincter, which is in this case laid bare by the two incisions (Inc) parallel to the anal orifice.

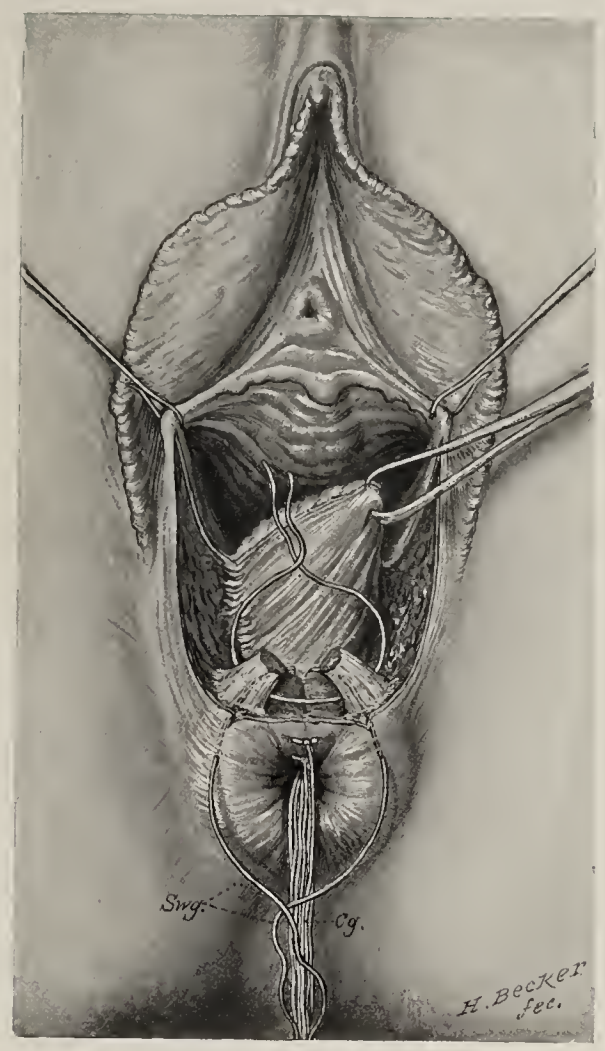


FIG. 7.—Denudation completed and rectal sutures tied, uniting the internal sphincter and radiating ont into the skin surface.

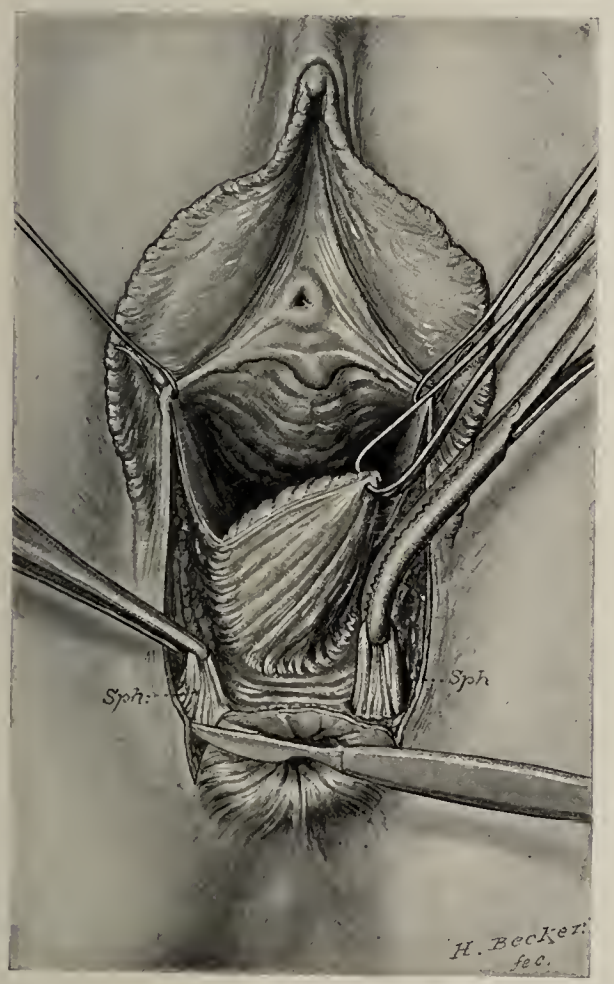


FIG. 6.—The incisions made as shown in Fig. 5 and the sphincter ends bared by dissection.



FIG. 8.—The rectal sutures all in place and the sphincter (Sp) ends united by 3 buried catgut sutures. A silkworm-gut tension suture passes through the centre of the sphincter muscle up around through the septum.

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My own method of treating the sphincter is similar to those detailed, in so far as the muscle is united directly end to end by means of buried interrupted cat-gut sutures, and I would prefer passing single sutures directly through the muscle to the use of tendon sutures, for the reason that the simple interrupted suture buries less foreign material, and it is therefore less liable to infection, lying as it does close under the skin.

The first essential point of difference between my own method and those of previous operators is a carefully conducted denudation, giving the sphincter a wider berth, so as to separate it from the skin surface, after all the parts have been brought into apposition, by a greater interval. This is done to make the burial of the cat-gut sutures a safer procedure.

The next important point is the dissection and liberation of the sphincter ends until one, or one and a half centimeters or even more are pulled out free on each side. This has not been proposed before. The ends are then cut off so as to remove the scar tissue and three interrupted cat-gut sutures passed through them so as to be ready to bring them snugly together at the proper time.

The rectal wound is then completely closed by a series of interrupted sutures passed close together so as to make it impossible for any minute particles of fecal matter to press between the stitches and cause an infection. This closure is carried down and over the anus onto the skin area, and then, only after this step is satisfactorily completed, are the sphincter ends brought together and the buried cat-gut stitches tied. Another point which I wish to urge, which differs from any previous proposition, is the passage of a silkworm-gut tension suture directly through the substance of the sphincter muscle half way between its outer and inner borders. The purpose of this suture is to take the tension off from the buried cat-gut sutures during the healing process. I prefer this suture to the Emmet tension suture which is passed well behind the sphincter ends on the skin surface, because my suture acts more directly and does not tend to make the anal orifice so small; it is therefore easier to secure earlier and regular defecation.

I have dwelt thus far upon the method of securing immediate union of the external sphincter muscle; it is my desire now in conclusion to insist upon the importance of paying equal attention to securing accurate approximation of the internal sphincter muscle. Indeed, if I would establish any comparison between the two, I would attribute more importance to the accurate union of the internal sphincter than to that of the external. This must be effected in the following manner: One or two fingers are passed into the torn bowel and the thin septum is brought slightly forward, while with a knife or a pair of scissors the operator splits the septum on its mucous margin and then dissects upwards and inwards, separating the vagina and its columna from the septum in such a way as to isolate the rectum in front and on the sides. By taking a little care and observing the tissues closely, the bowel with the muscle is easily set free, and if the dissection is well done the internal sphincter fibres will be clearly recognized on both sides.

After all the scar tissue is removed the internal sphincter is then united by a series of interrupted fine silk sutures entering and emerging on the mucous surface of the bowel about a millimeter from the edge of the cut. These sutures are passed and tied from above downwards from one and a half to two mm. apart; in a case recently operated upon I used as many as sixteen of them before the bowel was closed down beyond the external sphincter.

I believe it is best to reinforce these rectal sutures by two or three cat-gut sutures buried in the septum above them and grasping the muscular coat of the bowel, that is to say, the internal sphincter, and drawing it together over the line of union established by the first set. After doing this the external sphincter is brought together as described above, and the remaining perineal and vaginal portions of the wound united as described in the text-books. The utmost care must be taken throughout not to leave any dead spaces in the septum or about the buried sutures.

After such an operation it is my practice to open the bowels at least every other day by giving a warm oil injection through a soft catheter.

NOTE.—I have received a communication from Dr. J. M. Baldy, of Philadelphia, under date February 9, 1899, in which he refers in detail to his own practice of suturing the sphincter muscle directly in the following language:

"As to the method I am using, at first I made a partial ligation of both ends of the muscle, after dissecting them out and freeing them for a quarter of an inch from all attachments. After securing the muscles with catgut the balance of the operation was performed like Emmet's. I found in several cases that the ends of the muscle sloughed—one case resulted in a cure, another did not, and I had to do it over. Consequently I changed the method to a simple suture of the ends as I would suture the ends of anything else, ligating as it were only one side, so as to give more security in holding the ends together, and at the same time save the chance of cutting of the muscle circulation and producing a slough. Then I finish as an Emmet, passing the lower sutures (silkworm-gut) through the sphincter far below the points of union so as to take off all tension from the catgut in the muscles.

When I get a very tight sphincter (or anus) I slip a small subcutaneous knife into the tissue at the posterior margin of the anus and sever as many of the sphincter fibres posteriorly as it is necessary to allow me to stretch the anus sufficient to give a free opening—that is, enough to allow the easy passage of my thumb. I always stretch the torn sphincter before beginning any denudation or dissection whatever.

The patients have sure and absolute control before they leave the Hospital. It is a big improvement over the old methods."

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ABERRANT PORTIONS OF THE MÜLLERIAN DUCT FOUND IN AN OVARY.*

By Wm. Wood Russell, M. D., *Associate in Gynæcology, Johns Hopkins University, Baltimore.*

The specimen which I present this evening is of extreme interest, because it brings up the much-disputed question as to the derivation of the gland-like spaces as well as the papillary and adenomatous tumors of the ovary: whether they take origin from the germinal epithelium, the remains of the Wolffian body, or the Graafian follicle. In the light of our present knowledge of the development of the urogenital system I am actuated, from the study of this specimen, to add another possibility to these just mentioned.

Accepting the studies of Nagel, that the epithelial elements of the Müllerian duct are derived from the germinal epithelium, as correct, I believe we are able to explain the condition found in this instance as due to an anomalous point of development of portions of the Müllerian duct in the germinal epithelium.

The ovary from which the slides were taken was removed January 2d, 1897, during an operation for a cystic adenocarcinoma of the left ovary.

As is the custom after removing a pelvic tumor, the other pelvic organs were inspected, and in this case I found the opposite ovary enveloped in adhesions on the posterior surface of the broad ligament, while the tube was free and patent. The patient having reached the age of the natural menopause, I decided that it was best to remove it, to relieve her of any future anxiety. Nothing unusual was noticed about the ovary, it being of normal size, the outer pole cystic and the surface covered with shreds of adhesions. The uterus was also normal.

The specimens were hardened in Müller's fluid, cut, and stained with hæmatoxylin and eosin.

On microscopic study of the right ovary, we were astonished to find areas which were an exact prototype of the uterine glands and interglandular connective tissue. Further search through serial sections of the remainder of the ovary revealed similar foci scattered throughout the specimen in which the glands and interglandular connective tissue were in many places surrounded by bundles of non-striped muscle. On the posterior surface at a considerable distance from the hilum, was a shallow groove partly filled with glands of the uterine type, opening on the abdominal side. The epithelium covering this group gradually merged into a single layer of low columnar cells and at the edges of the groove spread out over the surface for a short distance as the germinal epithelium.

A large corpus luteum which occupied the outer pole was two-thirds surrounded by a narrow space lined with columnar epithelium. In places this epithelial lining dipped down into the tissues beneath, and formed gland-like structures.

In the substance of the ovary were spaces lined with columnar epithelium in places having distinct cilia. Beneath this was a band of glands imbedded in connective tissue. The glands were arranged as in the normal uterine mucous membrane and opened into the spaces, their epithelium being continuous with its lining membrane. The interglandular connective tissue was composed of small cells with darkly staining oval and round nuclei almost completely filling the cell body, in fact identical with that found in the uterus.

Beneath the spaces were bundles of muscle, arranged more or less concentrically, with strands running off into the ovarian tissue.

Leucocytes and red-blood corpuscles with indistinct outlines partly filled the spaces. The whole formed an exact reproduction of a portion of the uterine mucous membrane and muscle. The arrangement of these structures gave the impression that they were a continuous system from the groove (Plate I, Fig. 3) on the posterior surface to a cystic space in the anterior face (Plate II, Fig. 2).

The ovary contained many corpora fibrosa and a few Graafian follicles in various stages of development; some of which were cystic. In many places throughout the specimen were foci of pigment in the ovarian tissue, in some of which the shrunken forms of red-blood corpuscles could be seen, being evidently the remains of hæmorrhage. The hilum did not contain any of these glandular structures, but appeared normal, except for a sclerosis of the vessels.

Williams[1] remarks, concerning the origin of epithelial elements, in the ovary: "Indeed, the number of theories advanced has been limited only by the number of structures entering into the composition of the ovary." I will not attempt, therefore, to review the subject, but state briefly the most important of the theories.

Germinal Epithelium.—Anomalies of growth in the germinal epithelium have, in many instances, been held responsible for these structures.

Waldeyer's[2] conception of the origin of the Graafian follicle, from nests of cells forming in the germinal epithelium and then being isolated from the other cells by connective tissue penetrating the area from below and surrounding these nests, is now accepted by, practically, all recent observers.

The Valentine-Pflüger theory which ascribed the origin of the Graafian follicle to specialized tubes, the so-called Pflüger's ducts, formed by the germinal epithelium dipping down into the substance of the ovary has therefore lost its significance, and the hypothesis dependent on it for an explanation of the origin of epithelial tumors of the ovary should be discarded.

In a later investigation Waldeyer decided that these gland-like spaces were accidental inclusions of germinal epithelium occurring either in fœtal or adult life.

Marchand[3] was the first to call attention to the close relationship between the germinal epithelium and the epithelium of the Fallopian tube, stating that primarily they have a common point of origin. He believed that the epithelium of the tube could extend out over the surface of the ovary, and by penetrating the stroma of the ovary produce tubules similar to

* Read before the Johns Hopkins Medical Society, April 4, 1898.

Pflüger ducts. From these, he argued, cysts might arise, and he further remarks on the histological resemblance between the mucous membrane of the tube and papillary tumors of the ovary.

Williams also traced a small papillary cyst in the ovary to a prolongation of the epithelium from the tubo-ovarian fimbria.

Shortly after the appearance of Marchand's paper, DeSinety and Malassey[4] described some interesting specimens in which they discovered tubes lined with epithelium running in various directions through the ovary and opening on the free surface, the epithelium at these places being continuous with the germinal epithelium. They considered these structures as analogous to Pflüger's duct, but formed in adult life. Since then, these observations have been frequently confirmed.

Nagel,[6] Gusserow and Eberth[7] believe that the germinal epithelium may be incited to papillary growths by inflammatory reaction about the ovary, Nagel having seen the germinal epithelium preserved beneath adhesions.

Graafian Follicle.—From the beginning of the scientific investigation of the genesis of ovarian tumors the Graafian follicle has played a prominent rôle. Frommel[5], in 1890, formulated a hypothesis, but was unable to prove it by actual finding. He had found a superficial papilloma of the ovary, which undoubtedly sprung from the germinal epithelium, and believed from this that the membrana granulosa of the Graafian follicle, being a derivative of the germinal epithelium, could produce similar growth.

Williams in 1894 found in what he considered a dilated Graafian follicle a papillary outgrowth from the membrana granulosa. Yet the question is by no means definitely settled that the membrana granulosa is a derivative of the germinal epithelium. Waldeyer's theory undoubtedly explains the manner in which the ovum becomes embedded in the ovarian tissue, but whether the cells lining the follicle are epithelial or connective tissue in origin remains unsolved.

Wolffian Body.—The Wolffian body, on account of the proximity to the ovary in the early development of the urogenital system, has been offered by many writers as a probable source of these glandular structures, but of this there is absolutely lacking scientific proof. The possibility that some of the tubules of the primitive kidney may be caught in the germinal epithelium while it is budding out to form the ovary cannot be denied, but I believe that if such an event should occur these tubules would retain their original characteristics and not be transformed to the type of those arising from the Müllerian duct.

Müller's Duct.—Recently, Kossman[8] has, with great skill, discussed the subject from a new aspect in connection with his work on accessory Fallopian tubes. He insists that all intraligamentary cysts reaching considerable size spring from rudimentary tubes lying in the broad ligament, which he has found to exist in about ten per cent. of women. His arguments which appear most plausible are as follows:

The secreting portion of the primitive kidney, the glomeruli, disappears completely during intra-uterine life and may, therefore, be left out of consideration. The parovarium, paroöphoron and Gartner's duct are simply conducting channels during fœtal life, and their epithelial lining has at no time in their history secretory power. If it had, they would sooner or later all become cystic, as they have no external openings. On the other hand, the mucous membrane of the tube has undoubtedly the power of secretion, and by occlusion of its openings always forms a cystic tumor, hydrosalpinx. He draws a sharp distinction between the embryological germinal epithelium during the formative stage and that of a later period. After the differentiation of the epithelium into its various parts, these specialized parts are entirely distinct in their character and without power of further reproduction. The germinal epithelium, after the developmental stage, remains functionally inactive and exists only as a single layer of epithelial cells covering the surface of the ovary.

All tissues of the body are subject to the rule that after differentiation has once taken place in fœtal life, one can never be transformed into another. Further, the papillary growth covered with ciliated cylindrical epithelium has, in this region, its only analogue in the tube. This holds good for the tube, ovary and broad ligament. Those arising in the ovary are from isolated plaques of epithelium of the fimbriated end of the tube which have become differentiated from the germinal epithelium at an abnormal point.

At this point it is important to understand the present views in reference to the origin of the epithelium of the Müllerian duct.

There has been a wide diversity of opinion on the subject, and several theories advanced, some believing that it is derived solely from the Wolffian duct, others from a specialized portion of the peritoneum, and yet others, partly from the germinal epithelium and partly from the epithelium of the Wolffian duct. To Waldeyer belongs the credit of first calling attention to the formation of the groove in the germinal epithelium which later becomes the Müllerian duct. Its significance, though, was not fully estimated until the appearance of Nagel's[9] work, who substantiated Waldeyer's observation, and further discovered that the germinal epithelium at the point contained the so-called sexual cells which are the progenitors of the ovules in the females. In following the further development of the Müllerian duct, he finds that the primitive groove closes at its distal end, forming a blind tube which sinks into the Wolffian body and pushes backward beside the Wolffian duct, but remains throughout absolutely independent of it.

The conclusion to be drawn from this is, that the epithelium of the Müllerian duct is exclusively derived from true germinal epithelium.

If we accept this view of Nagel it is not difficult to conceive that a portion of germinal epithelium, which forms the ovary should, at times, attempt to produce structure which its function elsewhere calls upon it to do.

Such an accident may be represented by simple tubes or spaces lined with ciliated columnar epithelium of the tube, or villous and papillary growth analogous to the mucous membrane of the tube or even the more complicated structure of the uterus, glands, interglandular connective tissue and muscle.

In the specimen which I have described there is a collection

of glands in a groove on the surface of the ovary. The epithelium covering them is continuous with a single layer of columnar cells at the margin of the groove and extends a short distance over the surrounding surface. Thus we have direct proof that the germinal epithelium is capable of producing glands analogous to those of the uterine mucosa.

Burkhard[10] has described a very interesting small multilocular cyst of the ovary in which was found non-striped muscle and glands. On the surface of the tumor were several nodules made up of involuntary muscle, throughout which were scattered small round cysts lined with ciliated epithelium. He ascribes these structures to the germinal epithelium, but does not associate them with the Müllerian duct. He has neglected to describe minutely the character of the connective tissue immediately surrounding these structures and I am unable, therefore, to determine if the specimen resembles the above in that particular.

Since writing the above, von Franque[11] has published the preliminary report of an ovary which apparently confirms the Wolffian body theory. His remarks are so brief that one is not justified in criticism, but it would seem that he has in his case positive evidence that the parovarial tubules can, as we have already suggested, enter the ovary through the hilum and produce these glandular formations.

I shall be able in a short time to produce further evidence that this theory holds good for the origin of epithelial tumors of the ovary, as I have discovered in the wall of the cyst of the opposite ovary structures identical with those described.

Discussion.

Dr. Barker.—The case is interesting to anatomists on account of its relation to the topic of the origin of the sexual ducts in man. In the development of the sexual organs of higher animals a curious transformation of organs used in other animals for very different purposes appears to have taken place. A comparison of the three pairs of kidneys of lower forms, the front, middle and hind pairs, and their special ducts with the structures met with in higher forms show that the ducts from the front pair correspond to Müller's ducts, those from the second pair to the Wolffian ducts, and those from the third pair to the ureters. The front pair of kidneys (Pronephros) never appear in human embryos, and yet strangely enough their ducts do appear. The middle pair of kidneys (Mesonephros) are represented in the human being by the Wolffian bodies; the third pair (Metanephros) are the functional kidneys of human beings.

Now as the need for more complicated sexual organs arose, it appears that the two front pairs of kidneys and their ducts were utilized to build them, those of the front pair being used for the organs of the female, and those of the middle pair for the genital organs of the male. The Müllerian ducts of the two sides ordinarily fuse in their lower two-thirds to form the uterus and vagina. The upper third on each side corresponds to the Fallopian tube of that side. In the male, the part corresponding to the Fallopian tube disappears; that corresponding to the uterus forms the *utriculus prostaticus*, the lower part disappearing entirely. In the female the Wolffian body, or middle kidney, is embedded as the paroöphoron in the hilus ovarii, the little ducts going to form the parovarium and the lower portion constituting Gartner's duct or the ductus epoöphori longitudinalis, a little tube which runs parallel to the vagina. In the male the Wolffian body (Mesonephros) is represented by the paradidymis or organ of Giraldès. The Wolffian duct gives rise to the ductuli efferentes testis, the epididymis, the ductus deferens, the ductus ejaculatorius and to the vesicula seminalis with its ductus excretorius. It seems likely that Skene's tubules in the urethra of the female are derived from the Wolffian duct in which event they might, perhaps, be fairly looked upon as the structures corresponding to the seminal vesicles and ejaculatory duct of the male.

The study of the embryology of these structures is essential for a clear understanding of the normal anatomy, and especially for the comprehension of the deviations from the normal mode of development met with in cases of hermaphroditism, etc. The pathology of various conditions first becomes luminous when the developmental relations are considered. The case which Dr. Russell has just reported would be extremely difficult to interpret had not the proximity of Müller's duct to the germ-cell masses been well established.

The case he has so carefully described is an extremely rare one, indeed I believe it is the only one on record. It is especially interesting that a portion corresponding to the uterus should be that which appears imbedded in the ovary.

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11. Von Franque: Über Urnierenreste im Ovarium, etc. Sitzungs-Berichte der physikalich-medicinischen Gesellschaft zu Würsburg, July 7, 1898.



FIG. 1.—Natural size, showing normal tube with patent fimbriated extremity. Ovary posterior view with portion of adventitious capsule.

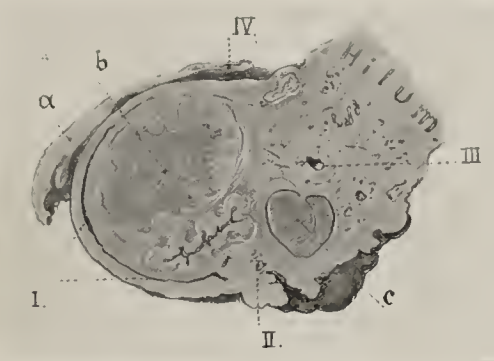


FIG. 2.—Longitudinal section through centre of ovary.

I. Space partially surrounding corpus luteum (*b*) lined with epithelium, in which on lower side glands were present.

II. Groove, at bottom of which is a wedge of tissue made up of glands and interglandular tissue covered with a single layer of epithelium continuous with that on the surface.

III. Space lined with columnar epithelium and surrounded by mucous membrane of the uterine type and non-striped muscle.

IV. Point beneath adhesions, (*a*) where germinal epithelium was preserved. (*c*) Cystic follicle.



FIG. 3.—Longitudinal section through ovary and hilum posterior face. (Magnified four times.)

I. Corresponds to I, Fig. 2. In the lining of the space toward the centre of the ovary is seen distinct gland formation.

II. Corresponds to II, Fig. 2, in which the glands can be plainly seen, some of which are cystic.

II′–II″. Groups of glands near surface of ovary surrounded by distinct stroma of uterine type.

III. Space surrounded by mucous membrane and muscle, an exact prototype of the uterine mucosa and muscle, some of the glands cystic, corresponds to III, Fig. 2.

IV. Germinal epithelium in adhesions. (*a*) Adhesions forming capsule. (*b*) Corpus luteum. (*c*) Cystic Graafian follicle. Right corner of section represents vascular zone of hilum, entirely free from glands.

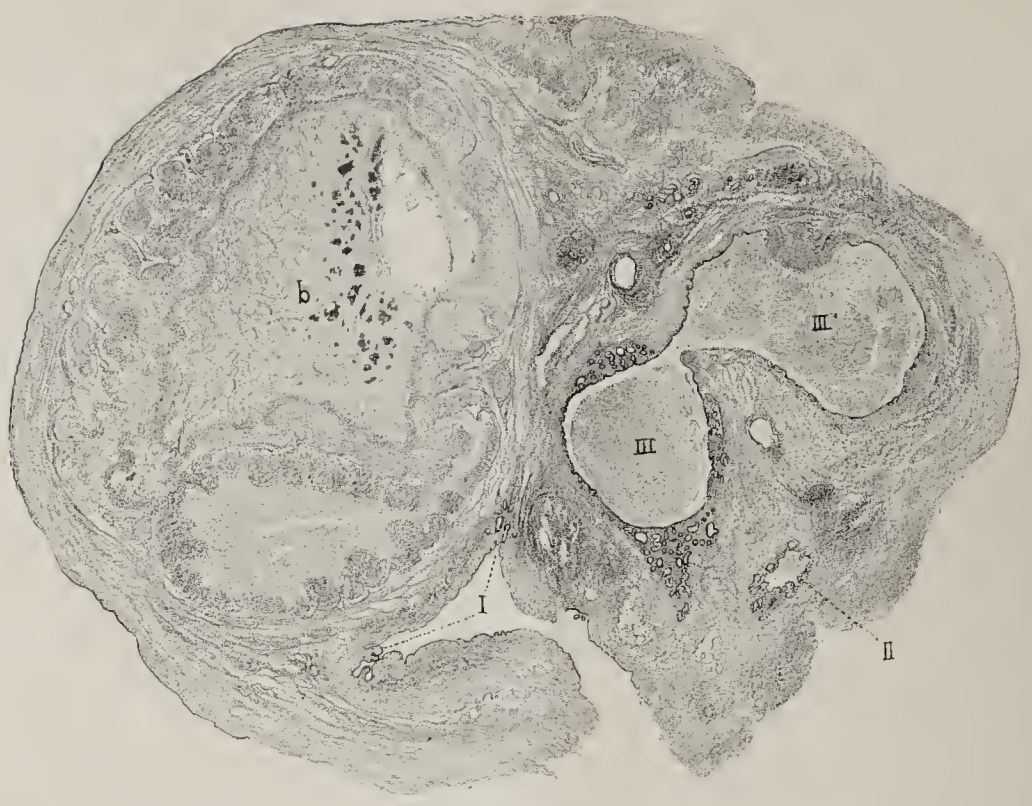


Fig. 1.—Longitudinal section through centre of ovary without hilum. (Magnified four times.)

I. Groove deseribed in Plate I.

II. Glands surrounding space near the capsule with stroma.

III–III′. Two large spaces in centre of ovary communicating by a narrow strait.

III. Space completely surrounded by mucous membrane and muscle, and lined with columnar epithelium, which is in places ciliated. The membrane becomes thinner as it approaches the strait, and just as it passes over into space III′, becomes a single layer of columnar epithelium.

Space III′. The cells forming its lining become gradually lower, merging first into cuboidal, and at the furthest point from the strait are flat. The knot-like projection in upper border of III′ is an organizing blood clot, covered at the base by flat cells. (*b*) Corpus luteum.

The contents of the spaces are made up of partly disintegrated red-blood corpuscles, leucocytes and granular debris.



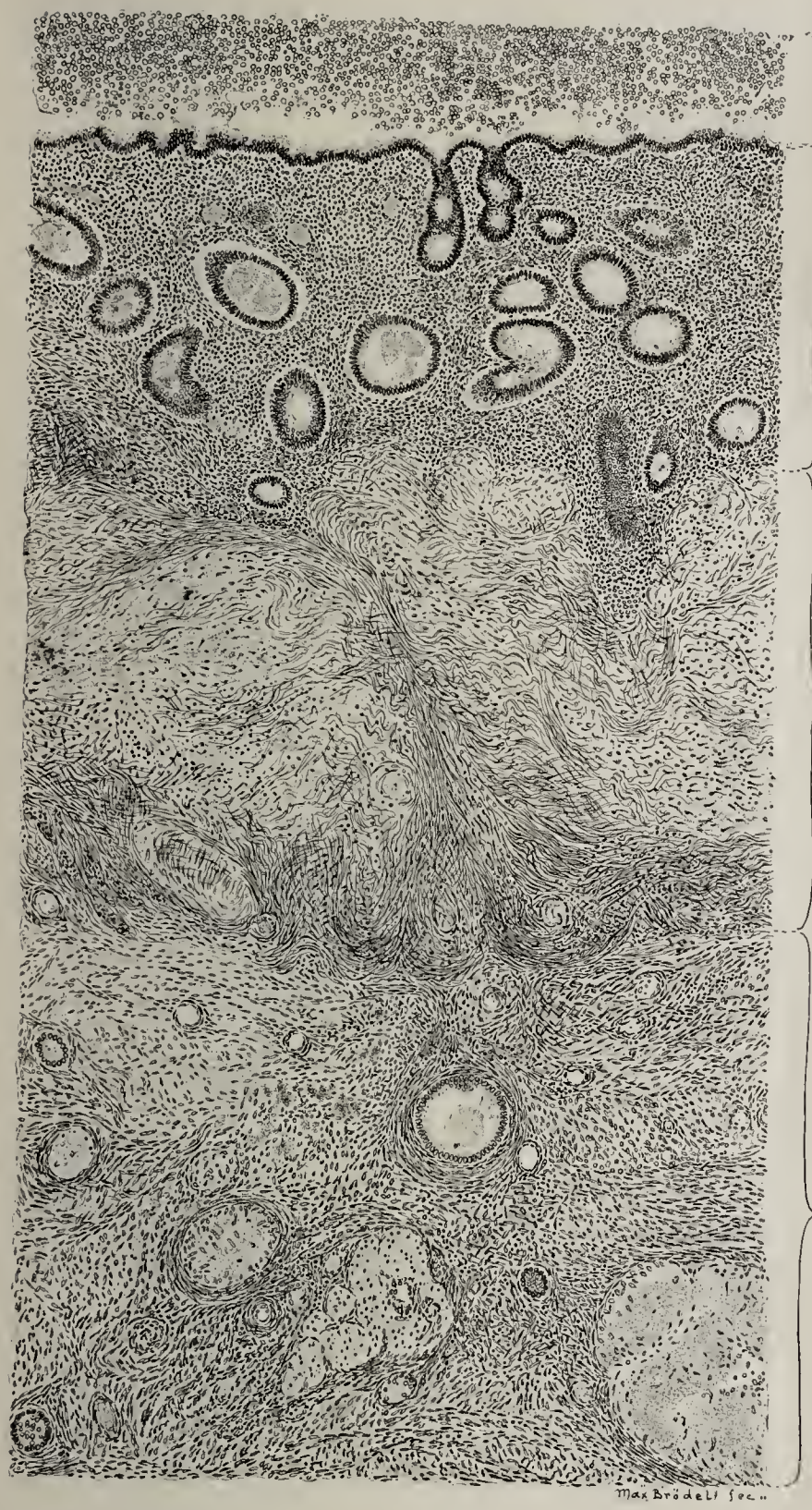
Fig. 2.—Longitudinal section through anterior face of ovary. (Magnified four times.)

I. Space in lower border of parenchyma of ovary lined with columnar epithelium, in which, at places, is distinct gland formation.

II. Groups of glands in and beneath capsule.

III. Large cystic space surrounded in greater part by connective tissue of the type found in the uterine mucosa. Most perfect glands along the left upper border.

III[1]. Group of glands. (*b*) Corpus luteum seen in other sections.



(*a*) Blood corpuscles forming part of contents of space.

(*b*) Typical uterine glands and stroma, two of the glands opening into space, and whose epithelial lining is continuous with that of the space.

(*c*) Non-striped muscle resembling that of the uterine wall.

(*d*) Normal ovarian tissue containing Graafian follicles in various stages of development and corpora fibrosa.

Portion of wall surrounding space III, Plate II, Fig. 1 (magnified 75 times), section through mucous membrane and muscle down into normal ovarian tissue.

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THE CAUSE AND SIGNIFICANCE OF UTERINE HEMORRHAGE IN CASES OF MYOMA UTERI.

A STUDY BASED UPON THE ARTIFICIAL INJECTION OF TEN SPECIMENS OF MYOMA UTERI AND FURTHER VERIFIED BY THE CLINICAL AND PATHOLOGICAL REVIEW OF ONE HUNDRED OTHER CASES.

By J. G. Clark, M. D., *Associate in Gynecology in the Johns Hopkins University, late Resident Gynecologist in the Johns Hopkins Hospital.*

Some three or four years ago, on searching through the current medical literature and the generally accepted text-books for an explanation of the hemorrhage so frequently accompanying myoma uteri, I was surprised to find very little unanimity of opinion upon the subject. Many writers merely state that hemorrhage is a frequent clinical symptom of these tumors, but attempt no explanation of this phenomenon. Others make the more definite statement that hemorrhage is less frequent the further the tumor is situated from the uterine mucosa, while still others quote the explanations of Wyder, v. Campe, Schmal and Semb, to which I shall refer later. With a view therefore of throwing more light upon this subject or at least of confirming the results of some one of the preceding investigators, I began the study of the macroscopic appearances in conjunction with a close analysis of the clinical history of specimens of myomata removed by hysterectomy. The observations, however, upon which I have relied most for my conclusions have been made in a series of ten artificial injections of the principal varieties of tumors. In my early study of these cases the fact had frequently impressed itself upon me that the mere size of the tumor bears absolutely no relationship to the amount of hemorrhage, for in some instances tumors as large as the pregnant uterus at term have been accompanied at no period of their development by this symptom, while, on the other hand, tumors so small as not to be perceptible to the patient have induced such excessive bleeding as to require operative treatment most urgently. Again the frequency of hemorrhage accompanying the submucous tumors and its absence in the subperitoneal types was self-evident.

In view of these general observations and the fact that on section myomatous tumors as a rule show a very poor vascularization, the explanation of the hemorrhage did not appear at first sight to be due to the tumor *per se*, but to mechanical disturbances induced in the uterine circulation through its presence. Myomatous tumors, as is well known, present a most remarkable morphological diversity; their size, form and position being subject to the widest variation from any fixed standard of development, due not to deviations from their primitive histological basis, for within narrow limits they conform more or less closely to a uniform microscopical type, but to variations in their gross anatomy. For clinical purposes these tumors are classified according to their location into subperitoneal, interstitial and submucous varieties, but comparatively seldom do we find a given specimen composed solely of any one of these types, for they are usually scattered indiscriminately throughout the uterine wall, some appearing as subperitoneal bosses, others as rounded nodules completely surrounded by uterine muscle, while still others project into the uterine cavity as submucous tumors.

Besides this multiplicity frequently single tumors are observed which partake more or less of the characteristics of all the other types; thus an interstitial tumor may project into the uterine cavity and besides present an equally extensive surface beneath the peritoneum.

In view of the heterogeneous growth of these tumors it would appear evident that any rule governing the hemorrhage which has a mechanical basis for its support must present many variations. The atypical bleeding in cases of myoma uteri may manifest itself therefore as an increase in the catamenial flow or as profuse and irregular inter-menstrual hemorrhages. Were the tumor itself to possess inherent characteristics which induce hemorrhage it goes without saying that in all cases this symptom would occur.

The splendid collection of myomata in the Gynecological Department of the Johns Hopkins Hospital contains one specimen which illustrates especially well the fallacy of the latter hypothesis. The tumor, a picture of which has already appeared in Kelly's Operative Gynecology, Vol. II, opposite p. 382, is a large angiomatous myoma, occupying the wall of the uterus but not impinging upon the mucosa. Notwithstanding this excessive vascularization the patient did not suffer from hemorrhage and came to operation simply on account of the steady increase in the size of the tumor.

Accepting as an axiom that "to determine the abnormal one must know the normal," it appeared to me absolutely essential to ascertain first the normal scheme of the uterine circulation before attempting to arrive at any conclusion concerning the changes induced in it by the growth of myomatous tumors. The following brief consideration of this subject will therefore not be out of place, for in addition to rendering an explanation of the atypical hemorrhages occurring in cases of myoma uteri easier, it also demonstrates the fact that our preconceived ideas of the vascularization of the uterus drawn from text-books in anatomy and gynecology are in certain details fallacious.

The Normal Circulation of the Uterus.

In beginning the experimental injections of the uterus, I considered it essential to define the areas supplied by the four arteries (two ovarian and two uterine) terminating in the uterus.

The most commonly copied picture of the circulation is that of Hart and Barbour (Gray's Anatomy), which represents the uterine and ovarian arteries as a thick tortuous communicating system lateral to the uterine walls, giving off branches which in turn quickly break up into tiny vessels terminating in a fine capillary anastomosis in the median line of the uterus. From this cut as well as from the descriptions by the majority of writers it would appear that not only is there a

poorly vascularized median line, but that there is little if any commingling of blood from the two sides except through this capillary anastomosis.

This idea, as I shall show, may be demonstrated as erroneous by artificial injections of the uterus. In my first injection experiments I employed an aqueous solution of Prussian blue. Cannulæ were inserted into the two uterine and two ovarian arteries, and the injection was begun by forcing the fluid first into the uterine artery of one side. Before even the peritoneal covering of the uterus was darkened the injection fluid had rushed through the lateral communication between the ovarian and uterine artery, and began to flow from the ovarian artery, thus showing that there is absolutely no bar to the reflux of blood from the uterine to the ovarian artery or vice versa, and that under normal conditions of the circulation the cardiac force transmitted through the uterine and ovarian vessels must act conjointly in forcing the blood from the utero-ovarian circle lateral to the uterus into their ultimate terminals. Another phenomenon, which was especially noteworthy, was the rapid crossing over of the injection fluid to the opposite side of the uterus, where it escaped, not from the vein, *but from the uterine artery*, and only after the latter was clamped did the fluid begin to escape from the efferent vessels. From the initial point of injection the entire uterus was deeply colored with the blue solution, demonstrating the existence of a very easy communication between the myriads of vessels ramifying throughout the uterus. Whether this communication was established through capillaries or whether through the direct anastomosis of larger vessels, I was not able to determine from this experiment; but still clinging to the idea set forth in the text-books I was disposed to accept the first hypothesis.

Still with the intention of defining separate areas supplied by each of the vessels I resorted to the use of a granular injection mass, consisting of ultramarine blue suspended in 10 per cent. gelatine, knowing that the granules would only pass down to the capillary system but not through it. Upon attempting this I was surprised to find that the same phenomena occurred as in the first experiment, demonstrating beyond doubt that there is, in addition to the usual capillary communication, a direct arterial anastomosis between the intra-uterine vessels, which is not an insignificant one, but plays a most important part in the circulation of the uterus.

When I related the phenomena noticed in my first injections, conducted in the anatomical laboratory of the Johns Hopkins University, to Prof. Spalteholz of the University of Leipzig, I found him disposed to cling to the older opinions and to think that possibly there was some error in my injection technique. Later, however, when making injections of the uterus from which to have pictures drawn for his anatomical atlas, he obtained identical results, and will depict in his forthcoming volume a direct arterial communication between the two lateral utero-ovarian circulations.

When we consider the varying physiological phases through which the uterus passes (the most important of which—the puerperal state—is dependent upon an abundant and unfailing blood-supply), this provision of nature, whereby an easy communication is established between its four arterial sources, not only through a capillary system like that of other organs, but also through a more direct arterial anastomosis, appears to be absolutely essential. To leave the nutrition of any portion of this important organ to the care of one set of vessels, which might become impaired, would undoubtedly render it liable at any time to serious functional disturbances.

To briefly epitomize the results of my observations on the normal vascularization of the uterus, I would say that it consists of the lateral utero-ovarian anastomosis which give off excessively tortuous secondary branches, some of which penetrate the outer layers of uterine muscle and finally terminate as delicate twigs in the uterine mucosa, while others extend across the uterus and fusing with similar branches from the opposite side form direct arterial communications. From the latter, branches are given off which also penetrate the deeper-lying musculature and terminate in the mucosa. Beyond establishing the fact that there are direct arterial communications besides the usual capillary anastomosis and verifying the main points in the vascular scheme as depicted by others, I have not attempted to go, contenting myself for the present with a macroscopic study of the gross specimens and with the examination by means of a dissecting lens of thick sections cleared in xylol.

I hope to make a further communication upon the exact scheme of the circulation of the uterus at a future date.

The Mechanical Disturbances in the Circulation in Cases of Myoma Uteri.

From my study of the circulatory changes in uteri, the seat of myomata, I am convinced that the increased menstrual flow and atypical hemorrhages which are so frequently associated with these cases are dependent solely upon mechanical conditions, which induce first, a congestion of the deeper-seated muscular and endometrial vessels and this in turn to an increase or prolongation of the menstrual flow, and second, an actual derangement or disorganization of the vascular systems of the endometrium and of the tumor itself, through which atypical hemorrhages occur, varying in degree from a slight inter-menstrual discharge to a loss of blood so great as to cause the most prostrating or even fatal anaemia.

First, as to the part played by mere venous stasis in the production of the increased menstrual flow.

In its natural history the uterus after puberty passes through its successive menstrual cycles with the attendant sanguineous flow. According to some observers this flow is due to an actual rupture of the capillaries of the endometrium, while others believe that it occurs through a simple diapedesis. The latter view is held by Dr. Cullen, who has reached this conclusion after an extensive study of the endometrium in all of its normal and pathological conditions. According to my own observations I see no reason to doubt this conclusion.

With this well-sustained theory before us as a working basis the explanation of the increased menstrual flow in cases of myoma uteri is comparatively easy. In their early growth these tumors appear as minute whitish bodies lying in the depths of the uterine muscle. In all of my injected specimens the smallest tumors, some of them not larger than a pea, show a remarkably poor internal vascularization, in comparison with

the surrounding musculature. The tumor apparently starts as a whirl or kink in the fibres of the muscle, and is not, according to my observations, supplied by a central vessel, as stated by some writers, but derives its blood-supply from vessels coursing between the surrounding fibres. This insignificant initial wreath grows into a thick network of encircling vessels which send radiating branches into the interior of the tumor. In the progressive development of the tumor the increase in the blood-supply is not commensurate with that of the tumor, which leaves its center sooner or later more or less isolated from the peripheral source. With the increasing size of the tumor, it follows the simple mechanical law of pushing in the line of least resistance, and accordingly tends to move outward towards the peritoneun, or inward towards the uterine cavity. In case the surrounding resistance is uniform it naturally maintains its intramural position. *Pari passu* with the outward mobilization of the tumor the tendency to a disturbance of the circulation sufficient to create menstrual disorders decreases. Even when the tumor remains as a simple interstitial growth no subjective symptoms relative to the menses are, as a rule, noted. There are, however, some instances where, notwithstanding the fact that the tumor does not encroach upon the mucosa, the menstrual flow may be increased or prolonged, but, so far as my observations go, never to the extent of becoming irregular and profuse. This condition, I am convinced, may be explained upon a mechanical basis. In the quiescent state of the uterus during the inter-menstrual period, the vascular system around the interstitial tumor is only partially filled; but let this same system become distended to turgescence under the menstrual influence, and it goes without saying that the force exerted by the congested and contracting uterine walls against the more or less dense fibro-muscular tumor, which remains practically unchanged in its resistance, will retard the exit flow from the deeper veins lying in proximity to the uterine mucosa. As a result of this venous stasis, increased extravasation or diapedesis of blood occurs into the uterine cavity. If there is a multi-nodular conglomeration of tumors the crowding together of these resistant bodies may also tend very greatly to inhibit the recurrent flow between them, producing even a greater internal congestion than in the first instance.

Here, just as in other tissues, the arteries, on account of the greater thickness of their elastic walls and their constant pulsations, tend to overcome the surrounding pressure and maintain their patulous condition, whereas the veins, which are in many instances little less than flaccid venous channels, are subject to compression upon the resistant tumors. A simple mechanical reproduction of this condition may be made by grasping in the palm of the hand a hard ball over which is placed a soft rubber tube with water flowing through it. A light pressure, sufficient to retain the ball in the hand, will not retard the flow through the tube, but a stronger grasp at once partially or completely checks the flow. In the application of this mechanical principle to cases of myomata, two sets of tubes coursing over the hard ball represented by the tumor must be considered, one of which, the arteries, as already stated, are elastic and pulsating, while the other, the veins, are mere passive channels. In the increasing congestion of the uterus incident to the menstrual cycle, the arteries tend to resist the surrounding pressure and maintain their flow, whereas the veins may become compressed against the tumor, and as a result a venous stasis in the deeper-lying tissue of the uterus occurs with a consequent increase and prolongation of the menstrual flux.

With the passing of the menstrual cycle the arteries return to a passive condition when the veins again become sufficiently patulous to transmit the blood to the large efferent trunks, and the metrostaxis ceases only to be renewed again in the succeeding period as a prolonged but otherwise normal flow. To prevent misconception as to the frequency of this occurrence I would especially emphasize the clinical fact, that in the majority of cases of interstitial and subperitoneal tumors, even increased menstruation does not occur, which is explained no doubt upon the ground of a compensatory vascular adaptability.

While the blood-vessels in close proximity to the tumor may partially be blocked the anastomoses within the uterus are so perfect as to leave patulous many other equally easy avenues of escape for the venous blood. Therefore, even a decided increase, without further derangement in the menstrual flow, is nearer an exception than a rule, unless there is some impingement of the interstitial tumor upon the endometrium.

With the encroachment, however, of the tumor upon the uterine cavity a second and most weighty cause for the hemorrhage comes into action. As depicted in the normal scheme of the uterine circulation the vessels which supply the endometrium reach this point by penetrating the inner muscular coat of the uterus, where they freely anastomose with each other and finally terminate as delicate twigs surrounding the glands of the mucosa. Until this scheme is very much deranged or disorganized by the advancing myoma usually no serious disturbance in the menses, as stated above, will occur. When the tumor, however, reaches the mucosa the menses tend to become free and prolonged, due to a thinning of the mucosa and a coincident degeneration of the vessels which renders the usual diapedesis much easier or gives rise to an escape of blood through actual rupture of the capillaries. In this connection I may say that, according to the histological observations of my colleague, Dr. Cullen, the vessels of the endometrium are very resistant, and that in the earlier stage of encroachment of the tumor the increased flow occurs by diapedesis rather than by actual rupture. At first only the terminal twigs of the endometrium are involved, but later, as the tumor advances and the tension is increased the mucosa through gradual erosion assumes a white, glazed, parchment-like appearance, showing the deeper-lying vessels of the capsule of the myoma.

At this stage the mucosa may be said to have disappeared from the dome-like prominence of the tumor; but further back towards the base where the tension is less and the process of erosion has not occurred, a vascular halo, formed by the vessels of the mucosa, is usually seen. Often a cup-like depression is made by the advancing tumor in the opposite uterine wall in which one finds the vessels exposed in a similar way. From this endometrial zone I have seen occur in some

of my injection experiments the most active oozing. In the further expulsion of the tumor the vessels undergo actual necrosis along with the tumor, which renders them brittle and more liable to hemorrhage through extensive ruptures.

The ocurrence of large irregular inter-menstrual hemorrhages may be taken therefore as an almost invariable indication of the development of a more or less extensive submucous tumor. When the tumor has reached the point where its overlying mucosa has entirely disappeared the hemorrhage may become well-nigh constant, appearing as a continuous oozing, which is especially aggravated during the menstrual epoch. Should the case be allowed to follow its own course without operative intervention, the tumor may be expelled completely with subsequent restoration of the patient to health, or it may become the seat of an infection which terminates the patient's life; or finally through the profound anaemia produced by the hemorrhage death may occur either through exhaustion or from a terminal infection.

Analysis of the Clinical and Pathological Records of 100 Cases.

In order to verify and further sustain the conclusions drawn from my experimental study, to ascertain whether there are frequent or wide variations from them, I have analyzed as closely as possible the clinical and pathological reports of 100 other cases. The clinical symptoms were taken largely from abstracts made by Dr. Brown from cases operated upon in the Gynecological Department of the Johns Hopkins Hospital, while the pathological reports were abstracted from records largely made by Drs. Cullen and Herdon. Excepting those atypical cases of myoma, such as the adeno-myoma-diffusum benignum (Cullen) and those in which there is a coincident infection, from ordinary pyogenic organisms or from tubercle bacilli or where there exists a coincident association with carcinoma, I have found a surprisingly small variation. For purposes of analysis I have first tabulated the clinical symptoms after which the pathological reports have been appended. As these tables are too voluminous for publication I have endeavored to embody the results of this analysis in the form of schematized drawings, hoping in this way to make these statistics more available for study than were they brought together in the ordinary tabulated form.

Of the hundred cases, I have first classified those which conform to the simple types of tumors (subperitoneal, interstitial and submucous), but as these comprise only about one-third of the total number, the remaining showing combinations of the three, I have placed them under the two following headings: Combined interstitial and subperitoneal, and combined interstitial and submucous tumors. In the latter group several cases have also presented subperitoneal tumors, but as they practically play no part in the production of hemorrhage I have grouped them all under the one heading.

Schematic Drawings of 100 Cases of Myoma Uteri.

(See Plates.)

This analysis shows beyond doubt that the clinical statement concerning hemorrhage in myoma uteri made by some authors is based upon accurate observations.

Dudley,* of Chicago, has stated this in such a concise and clear way that I take pleasure in quoting it. He says: "The degree of hemorrhage depends upon the location of the tumors relative to the endometrium and the peritoneum.

The closer its relations to the uterine mucosa, the greater the hemorrhage; the nearer to the peritoneum the less the hemorrhage; hence menorrhagia is almost invariable with the submucous variety, less severe but very common with the intramural, and usually slight or absent with the subperitoneal.

The pedunculated submucous and the pedunculated subperitoneal myomata stand at the two extremes, the former producing the greater hemorrhage, the latter none at all."

The Surgical Aspect of this Study.

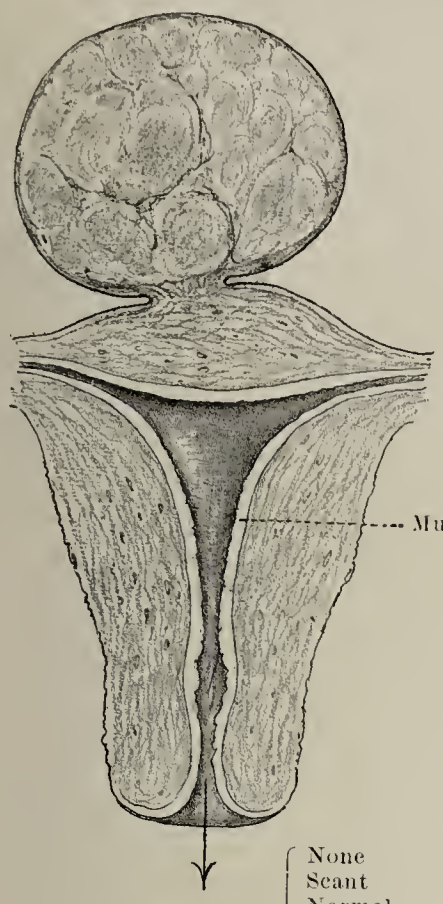
In criticism of the remarks following the appended reports of cases it may be said that an ante-operative judgment sufficient to render definite advice, as to the adoption of a radical or conservative line of treatment, is not possible, because data sufficient to support such a judgment cannot be obtained from the anamnesis or from our usual methods of examination. Admitting that this to a certain extent is true, I am nevertheless convinced that the close study of the symptoms in conjunction with a careful examination of these cases will usually yield very definite or at least strongly significant suggestions which will lead to a more complete diagnosis than is usually made.

The simple diagnosis of a myomatous tumor of the uterus with a subsequent hysterectomy is no longer a difficult matter, but the careful exclusion of the large number of cases from the great general class which, until the last two or three years, have been subjected to the wholesale extirpation of the uterus is a matter requiring accurate discrimination and good surgical judgment. Besides the superior judgment required for the selection of these cases, higher operative measures are brought into play, for it certainly requires more skill to remove the many tumors which one so often finds studding over the surface of the uterus, distending its walls or projecting into its cavity, and to repair through a plastic operation the resultant defects, than to perform a simple hysterectomy. The immediate results and splendid progress of these cases subsequent to operation are the strongest arguments in favor of conservatism.

The removal of either ovaries or uterus in young women, in the majority of whom the maternal instincts are more or less strongly implanted, is to my mind one of the most serious surgical procedures, and always to be avoided when possible, not because of the direct influence exercised by the presence of these organs on the womanly characteristics, but because of the depressing mental influences which follow in some instances the realization by the patient that she is sterile and will remain so to the end of her life. To say, therefore, that a simple or multiple myomectomy with the preservation of the ovaries and tubes is a great improvement over total hysterosalpingo-oophorectomy is not a subject for argument. It is a self-evident truth based upon the principle of preservation

* Diseases of Women, 1898.

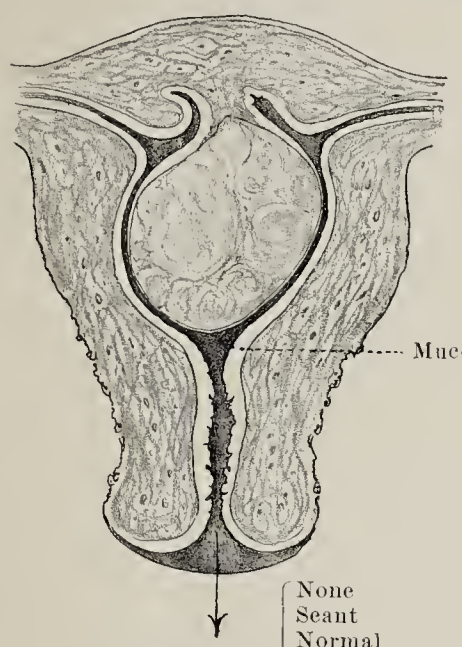
6. Subperitoneal.



Mucosa { Normal 4 / Thickened 2 / Atrophied 0

Menstrual Flow { None 1 / Scant 2 / Normal 3 / Profuse 0 / Irreg. and Profuse 0 / Continuous 0 / Painful { No 6 / Yes 0

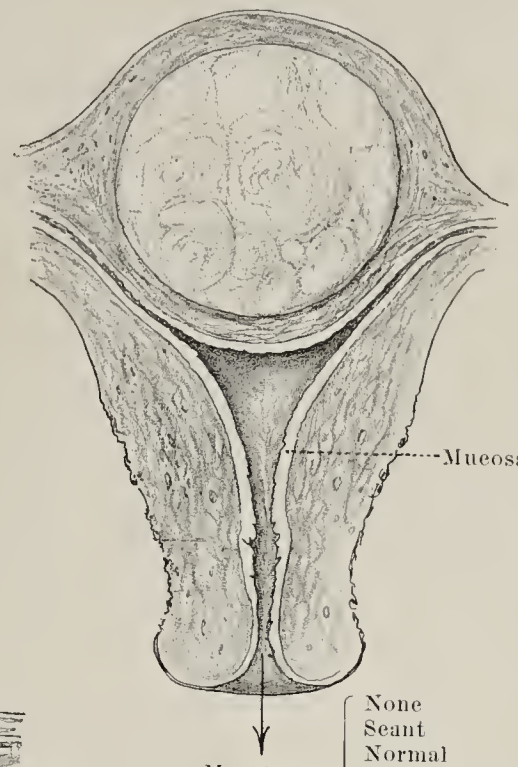
4. Submucous.



Mucosa { Normal 0 / Thickened 0 / Atrophied 4

Menstrual Flow { None 0 / Scant 0 / Normal 0 / Profuse 0 / Irreg. and Profuse 3 / Continuous 1 / Painful { No 3 / Yes 1

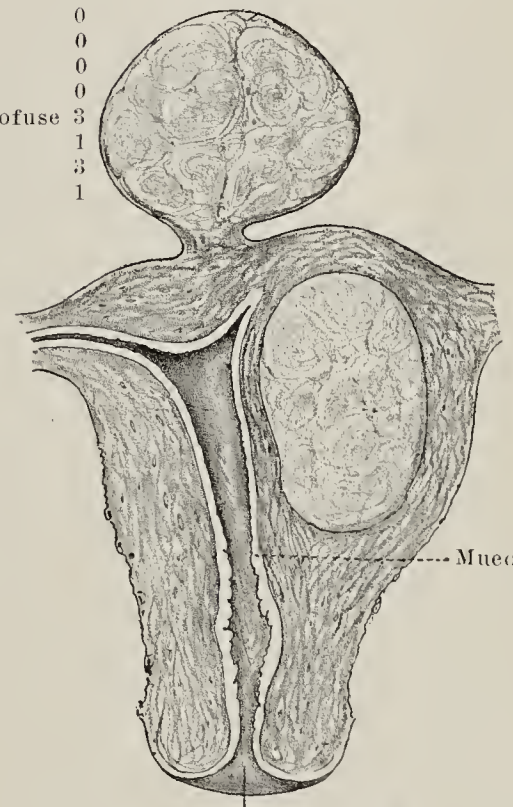
21. Interstitial.



Mucosa { Normal 9 / Thickened 4 / Localized 0 / Atrophied 8

Menstrual Flow { None 1 / Scant 1 / Normal 11 / Profuse 5 / Irreg. and Profnse 3 / Continuous 0 / Painful { No 8 / Yes 9

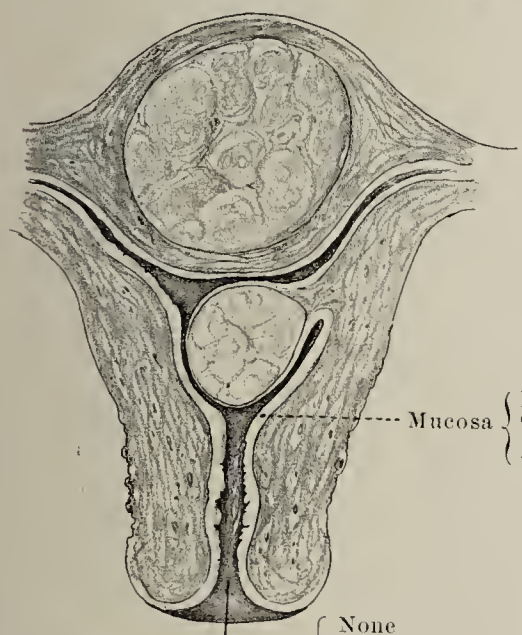
42. Combined Subperitoneal and Interstitial.



Mucosa { Normal 20 / Thickened 10 / Atrophied 12

Menstrual Flow { None 2 / Scant 4 / Normal 22 / Profuse 9 / Irreg. and Profuse 4 / Continuous 1 / Painful { No 21 / Yes 18

27. Combined Interstitial and Submucous.



Mucosa { Normal 1 / Thickened 1 / Atrophied 25

Menstrual Flow { None 0 / Scant 0 / Normal 4 / Profuse 10 / Irreg. and Profnse 10 / Continuous 3 / Painful { No 9 / Yes 14

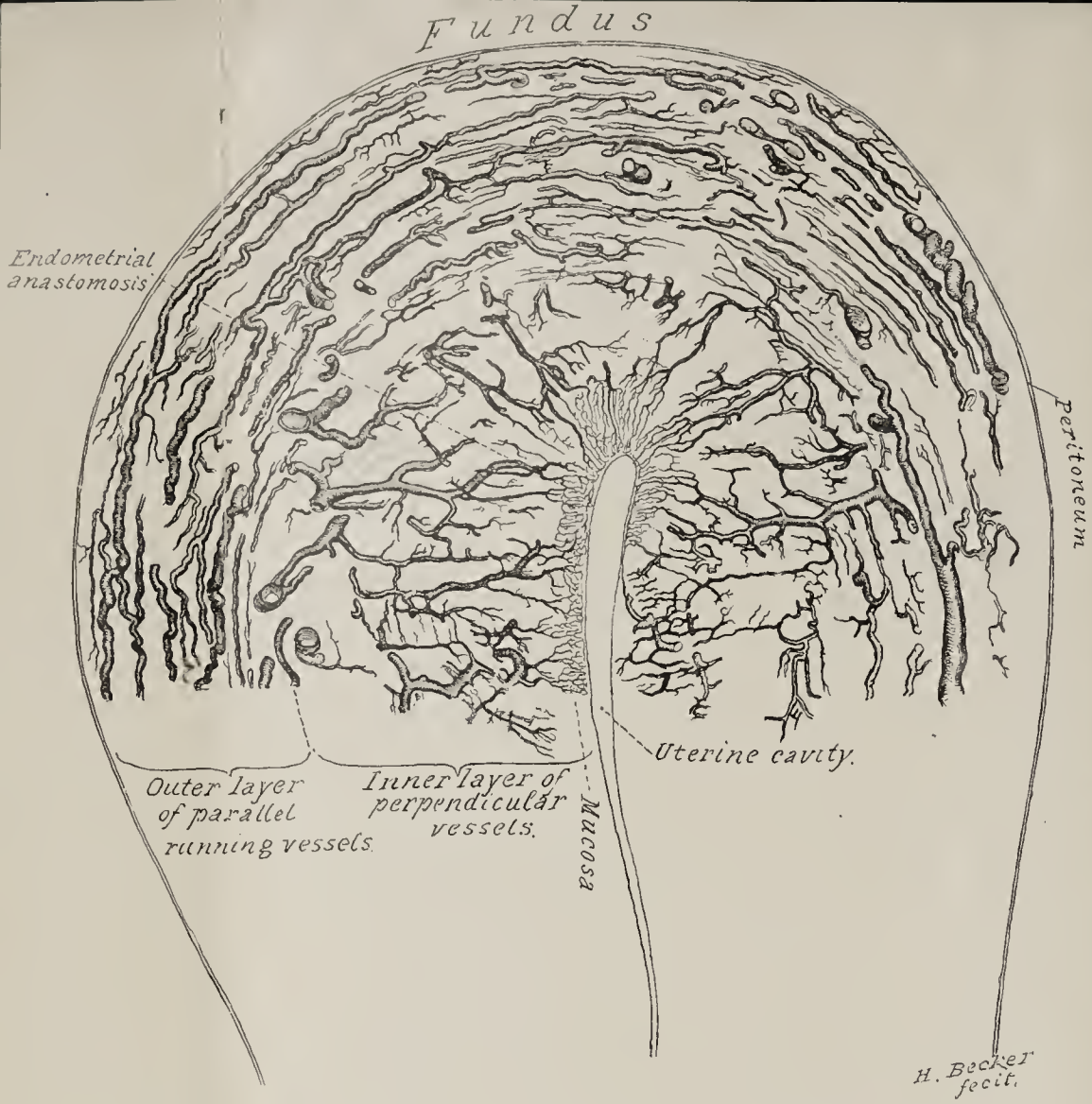


FIG. 1.—Sagittal section of uterus showing the scheme of the arterial distribution. The parallel vessels of the external muscular layer freely anastomose among themselves. From the innermost arteries branches are given off at right angles which penetrate the inner muscular layer, supplying it with numerous anastomosing nutrient vessels, and finally terminate in a rich capillary supply to the endometrium.



FIG. 2.—Injected specimen of interstitial myoma, showing derangement of vascular scheme. The perpendicular vessels noted in the normal scheme have here assumed a parallel course through the encroachment of the myomatous tumor. The endometrial twigs, instead of being merely the straight terminals of the perpendicular branches, are here given off at right angles. During the menstrual congestion these twigs naturally become more congested, through purely mechanical conditions, than in the normal state, consequently an increased diapedesis occurs. The large venous channels upon the surface of the myoma, to which attention has been called in the text, are also well shown.

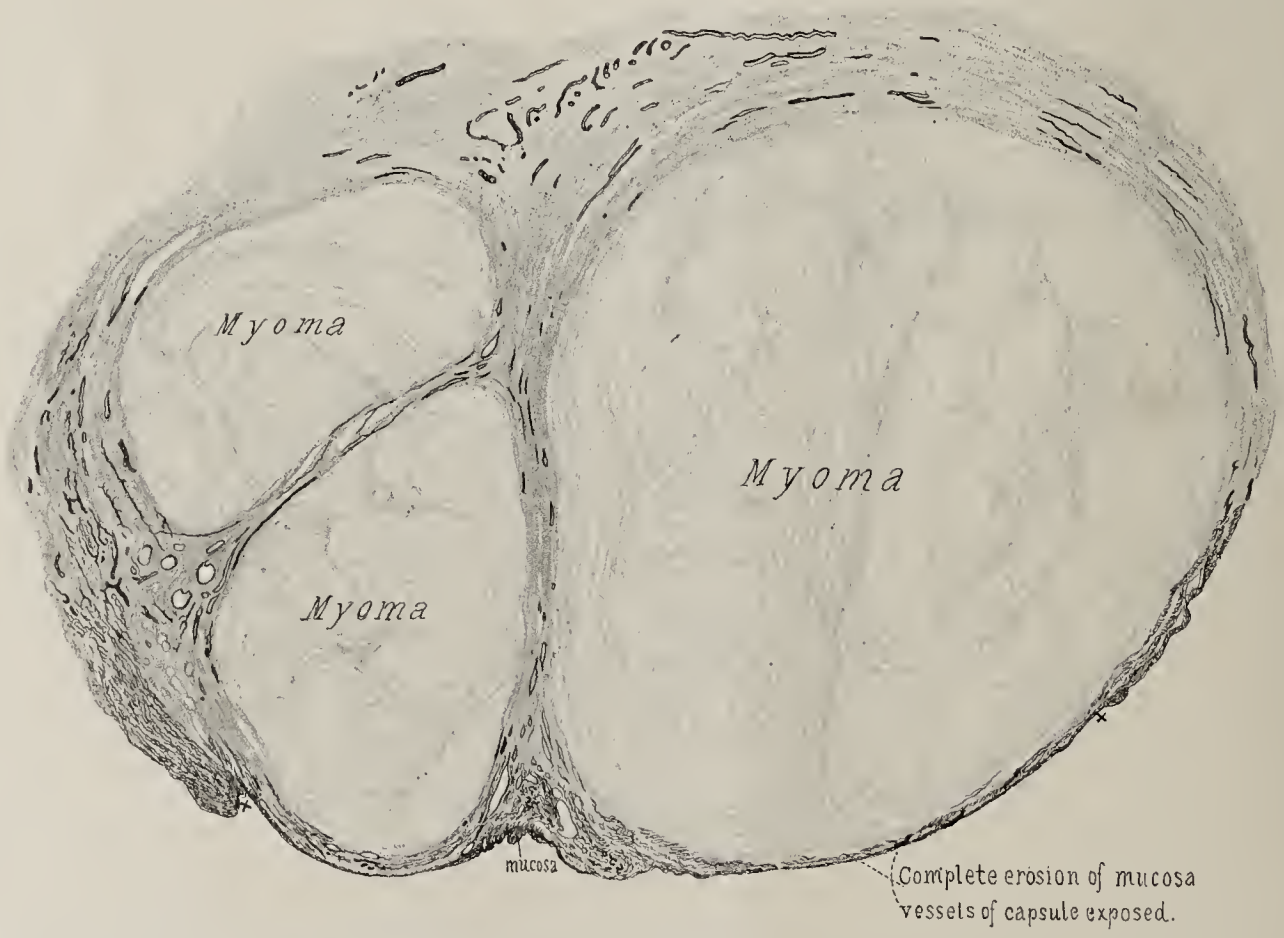


FIG. 3.—Uterine wall containing three interstitial myomata, two of which have so far encroached upon the uterine cavity as to cause almost complete erosion over the larger and considerable atrophy of the mucosa over the smaller tumor. The mucosa in the depression between the tumors is greatly thickened, œdematous and congested. Limit of mucosa indicated on either side by ×. In this instance the influx of blood being only slightly impeded and the reflux very greatly retarded by the crowding together of the three tumors the hemorrhage was excessive and irregular. The mucosa over the large tumor was so far eroded as to leave the wreath of vessels around the tumor exposed and subject to rupture either through simple pathological or traumatic influences.

rather than that of sacrifice, which in the end leads to a restoration rather than an abrogation of function. I feel assured when the combined statistics of the best surgeons of the world have been brought together after the general adoption of these revived principles, that those on conservative myomectomy will present a much more gratifying result than those on total hysterectomy.

A Brief Reference to the Literature Bearing Upon the Etiology of Hemorrhage in Cases of Myoma Uteri.

The almost unlimited and unclassified literature dealing with the subject of myoma uteri in its various aspects renders well nigh impossible a selection of the special work upon this topic. For this reason, therefore, I must disclaim the thought that this is an exhaustive review, for I have only attempted to give a brief abstract from those investigations which are generally quoted, with the view of calling attention to the most interesting and instructive points previously brought out in this line.

Wyder,* whose conclusions were drawn from the study of 20 cases, attributed the hemorrhage to endometritis, induced through the presence of the tumor. According to him the thicker the muscle which separates the myoma from the uterine cavity the less frequently will the circulation be changed and the more pronounced becomes the growth of the uterine glands without participation of the interglandular connective tissue. On the other hand, the nearer the tumor approaches the uterine cavity the more frequently occurs the growth of the interglandular connective tissue, which may leave the glands intact or induce complete atrophy.

Concerning the hemorrhage, he says so long as the endometritis which, according to his opinion, is a constant accompaniment of these tumors, is confined solely to the glands and the interglandular tissue remains approximately normal, this symptom will not occur, and it will only arise when both constituents of the endometrium undergo an increase (Olshausen's endometritis fungosa), or when the one or the other grows excessively, or finally when in addition to the endometritis glandularis there is also an interstitial inflammation.

As is at once evident, Wyder's views are not tenable, for, as stated by Semb,† the tumor cannot of itself induce an inflammatory process in the endometrium.

In the examination of 23 cases in Leopold's clinics Semb found in many instances absolutely no evidence of endometritis, and in those cases in which an inflammatory process occurred he considered it merely as secondary to the tumor. From his histological examination he concludes that the mucosa undergoes hypertrophy, without preceding inflammation, consisting either of a uniform increase in both the stroma and the glands or the glandular changes may predominate. After reviewing each of his cases he says hemorrhage will not arise, notwithstanding the most marked changes in the endometrium, or increase in the size of the tumor, if the walls of the tumor show no hypertrophy. According to this view therefore the hemorrhage depends upon hypertrophy of the uterine musculature with accompanying pathological changes in the vessels.

Schmal * arrived at the following conclusions concerning the changes in the uterine mucosa from the study of 15 cases: First, in subserous myomata the mucosa may remain normal or become hypertrophied. Second, in interstitial submucous tumors the mucous membrane becomes atrophic over the tumor and hypertrophic opposite the tumor. No opinion is expressed concerning the occurrence of hemorrhage in these cases.

Borissoff,† from a study of 21 cases of fibro-myomata, reached the following conclusions:

1. In fibro-myomata the mucosa shows a pronounced sclerosis, which in many cases induces a complete atrophy of the mucosa.

2. Glandular endometritis is relatively seldom observed. It occurs more often in combination with interstitial endometritis.

3. The influence of the tumor upon the mucosa depends entirely upon its position in the uterine wall and its size. If the tumor has reached a certain size it induces through mechanical influence a stretching and atrophy of the mucosa.

4. Bleeding from the uterine cavity results from stagnation of blood in the mucosa and occurs mostly *per rhexin* of the vessels which have undergone pathological changes.

5. The inflammatory changes in the mucosa with the congestion and hemorrhage lead to a desquamation of the epithelium.

Schauta,‡ at a more recent date, states in his text-book that hemorrhage seldom occurs from the myoma or its capsule; erosions of the covering layers of the tumor may, however, lead rapidly to fatal bleeding from the large sinuses. Changes in the mucous membrane play the principal rôle; of these hypertrophy takes a much less part than the degeneration of the mucosa and its vessels. This degeneration consists in a thinning, necrosis and erosion of the tense mucosa over the tumor as well as changes in the blood-vessels, which lead to the occlusion of some, to the widening of others and to the rendering of the loops of the vessels brittle.

To my mind this is the best concise statement of the subject which I have found, and conforms in general, as do the conclusions of Borissoff, with those which I have reached.

Cases Illustrating Mechanical Disturbances in the Circulation in Cases of Myoma Uteri.

A brief clinical report of the cases with the description of the injection experiments of the principal types of tumors will, I believe, be of more service in explaining the hemorrhages in these cases than the mere recital of results. I therefore offer no apology for inserting the following report of cases. For the sake of brevity I have reduced my notes to merely the essential points bearing upon the question, divest-

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* Archiv f. Gynaek., Bd. XXIX.
† Archiv f. Gynaek., Bd. XLIII.

* Archiv de Tocologie et de Gynécologie, Tome XVIII.
† Inaug. Dis.: "Ueber die Veränderung der Uterus-Schleimhaut bei Fibromyomen in Verbindung mit Uterusblutungen," St. Petersburg.
‡ Lehrbuch der Gesammten Gynäkologie, 1896.

ing them so far as possible of irrelevant and unnecessary matter.

Case I. *Menstrual history.*—Menses occurred first at 14 years, regular, accompanied by cramp-like pains, moderate flow, occasionally dark clotted.

Description of specimen.—Uterus converted into a smooth globular mass about the size of that of a three-months pregnant. The surface of the uterus is even and its general form has not undergone very much distortion, notwithstanding the presence of numerous interstitial nodules, which may be felt within the uterine walls. Posteriorly at the cervico-fundal juncture an interstitial tumor has pushed out towards the periphery and appears as a partial subperitoneal growth.

Injection.—Fluid carmine and granular blue injection mass. Cannulæ inserted into each ovarian and each uterine artery, the ovaries remaining attached to the tumor.

Injection began in the left uterine artery, when almost immediately the fluid imparted a deep red color to the uterine wall of that side; hardly had this occurred before the mass quickly passed through the uterus at the cervico-fundal juncture and began to flow from both the uterine artery and vein, followed quickly by its escape from the two ovarian vessels, necessitating the clamping of all of them. From this one vessel the entire uterus and Fallopian tubes were injected.

At the completion of the injection from this source, notwithstanding the apparent complete filling of all the vessels of the uterus, each of the three remaining arteries (one uterine and two ovarian) was in turn injected with a blue granular mass, when the same phenomena were repeated so far as the distribution of the injection fluid was concerned. By this time a very small amount of the red gelatine mass was flowing from the cervix, partly from the uterine cavity, mostly however from the severed ends of the small cervical vessels.

Examination of specimen.—On section through the uterus in the median line, from the fundus to the cervix, a most interesting picture is presented.

The uterine muscle is of a uniform red color, mottled with many blue points, indicating the branches of the arterial system. In the midst of this deep red ground color numerous paler myomatous nodules are seen, representing the various clinical varieties of these tumors. One interstitial tumor lies in close proximity to the mucosa. In color the myomata stand out in sharp contrast to the uterine wall, for they are universally poorly injected, the degree of vascularization however varying in the different tumors, some appearing of an alabaster-like whiteness and so poorly supplied with blood as to raise the question of how their existence is possible with so little nutrition. Others, however, are better provided with a vascular system. Of these one is especially interesting, for it is made up of two whirls of muscular tissue with a distinct septum between them carrying blood-vessels which send branches off into the adjacent nodules. Every nodule in the uterus appears well surrounded with vessels consisting in some instances of large open-mouthed channels which appear little less than venous sinuses. The peripheral nodules show a marked thinning out of the zone of vessels beneath the peritoneum, the main blood-supply coming from the vessels deeper within the walls of the uterus. The endometrium is deeply injected with the red gelatine, while numerous blue puncta are seen over the surface, indicating the terminal points of the arterial twigs.

A thin delicate film of red gelatine is spread uniformly over the mucosa, which has evidently oozed from the vessels of the endometrium. So far as visible pathological changes are concerned the endometrium presents nothing significant, being of normal thickness and consistence throughout the uterus, the interstitial nodule not yet having advanced a sufficient distance into the uterus to cause any visible changes.

Epitome of observations.—Universal injection of the uterus and tubes from one uterine artery; rich vascularization around and poor vascularization within the tumors; absence of extensive oozing into the uterine cavity, notwithstanding the presence of many intramural myomata; absence of gross pathological changes within the endometrium.

Case II. *Menstrual history.*—Patient is a colored woman of rather low intelligence and gives an indefinite history of her menstrual symptoms up to a few months ago, when the flow became profuse. Lately the hemorrhages have become excessive, reducing the patient to a very anæmic condition.

Description of specimen.—The uterus has been converted into an irregular tumor mass through which it has become so distorted that it no longer maintains any semblance to its normal form or size.

The main body of the uterus is very greatly enlarged and is studded over with subperitoneal tumors.

Upon the middle of the fundus a tumor the size of a fœtal head is attached by a thick fleshy flat pedicle. The surface of the tumor is of a dull grayish-white color, and shimmering through the peritoneal covering are yellowish necrotic-looking areas. On the left lateral wall there is a nodule about the size of a hen egg, which has undergone calcareous change.

Injection.—Carmine red and granular blue gelatine injection mass.

The left uterine artery was taken as the initial injection point, from which the entire left side became faintly red and then gradually spread upward through the fleshy pedicle of the large tumor and partially injected the peripheral areas.

Very soon after the beginning of the injection the fluid gelatine began to flow from the opposite ovarian vessels.

While injecting the second uterine vessel the fluid began to flow from the cervical canal in a large stream, showing that there must be extensive oozing within the cavity.

The ovarian vessels were injected in turn, at the completion of which the main body of the uterus and the base of the subperitoneal nodules were of a deep red color, but approaching the outer poles of the tumors the injection became fainter and fainter, until in some of them, especially the large and the calcareous tumors, there appeared to be a complete occlusion or destruction of the vessels.

Examination of specimen.—On section of the uterus a large submucous myoma 5x4 cm. was found covered by a fine leash of extremely thin-walled vessels varying from the size of capillaries to furrowed sinuses as large as a goose quill.

Numerous ruptures had occurred in these vessels as evidenced by the many areas where large exudations of fluid had occurred over the surface and by the large coagulated mass which filled the uterine cavity like a cast.

The endometrium appeared normal or hypertrophied, except over the tumor, where complete erosion had occurred, leaving exposed the capsule of the tumor with greatly dilated and thin-walled vessels running over its surface. On section the interstitial nodules presented the same appearances and poor vascular supply as noted in the preceding case.

The submucous and subperitoneal tumors show a marked variation in their vascular systems, due to the mobilization of the tumors from the interior to the surface of the uterus. In every instance the wreath-like arrangement has been destroyed, and the blood supply is obtained through the vessels traversing the pedicle or base of the tumors.

The center of the large subperitoneal tumor has undergone almost complete necrosis and consists of a cavity filled with a soft yellowish-white pulpy detritus, while one of the other nodules above noted has become calcified.

The center of the large submucous tumor is also of a very soft yielding brain-like consistence.

Epitome of observations.—Injection of well-nigh entire tumor mass from one uterine artery; full vascularization around but very poor within interstitial tumors; great failure in blood supply of subperitoneal tumors as a result of which one has undergone necrosis, the other calcification; complete disappearance of endometrium over submucous tumor and contiguous areas of the uterine wall; exposure of large sinuses within the capsule of the submucous tumor, with rupture of these sinuses and other smaller vessels; beginning degeneration of submucous tumor through failure of internal blood supply.

Remarks.—This specimen presents an interesting phase in the life history of myoma uteri, for it undoubtedly represents a stage in which the hemorrhage has reached its height.

Had this case been allowed to take its own course without the intervention of surgical measures, the subsequent history would no doubt have been marked either by death from acute anæmia or from a terminal infection, or by a complete extrusion of the submucous tumor, with a final cessation of the hemorrhage, for in this specimen there was no other interstitial tumor impinging upon the uterine mucosa, on the contrary they were all in process of mobilization towards the peritoneal surface.

The large subperitoneal tumor was already in an advanced stage of necrosis, and it is possible to conceive that notwithstanding the number and size of the tumors, a gradual decrease in size by slow absorption with final cessation of all threatening symptoms might have occurred.

In the days when these tumors were never operated upon, instances are recorded of large tumors disappearing which were no doubt of this character. It is of course a *reductio ad absurdum* to assume that the stone-like tumor would ever have disappeared through any disintegrating process, but it is not contrary to the natural history of these and of cases of lithopedion for calcified masses to remain *in situ* throughout the natural life of their hostess without inducing serious consequences.

These remarks are simply incidental and bear purely upon the supposititious terminations of such cases as these, and they are in no sense intended as suggestions for conservatism in their treatment. On the contrary, my views are radically in favor of nothing less than a total hysterectomy.

Even assuming that this post-operative knowledge might have been in the surgeon's possession at the time of operation, no other course than that pursued would have been advisable, for while the case might have terminated favorably under a conservative policy the dangers of a fatal hemorrhage, of a long drawn out illness from prolonged necrosis or from suppuration of the submucous tumor, of a rapidly lethal terminal infection, or of many other immediate or remote complications would have so far overshadowed this result as to make it extremely bad surgery to do less than perform a hysterectomy.

CASE III. *Menstrual history.*—Menses occurred first at 14 years, regular, accompanied by considerable pain; since onset of present disease the flow has been thinner and is more watery than usual.

Description of specimen.—Irregular multinodular myoma measuring 15 x 10 cm. in size. The uterus is so distended by the irregular growth and distribution of the tumors that it has lost all appearance of its original shape. The base of the uterus where it has been amputated is irregular and the uterine arteries stand out prominently as large patulous tubes. Two interstitial tumors have well-nigh reached the stage in their mobilization towards the peritoneal surface where they may be designated as purely subperitoneal. On palpation of the mass two or three large interstitial tumors may be outlined.

Injection.—Granular blue and red injection mass. The same phenomena were observed in the topographical distribution of color as in the foregoing experiments. On applying increased pressure to the injecting apparatus towards the close of the experiment the gelatine was seen flowing from the uterine cavity as a thin, delicate film.

Examination of specimen.—On section the uterine wall was found to be occupied by two large interstitial and three partially subperitoneal tumors. The uterine cavity was somewhat tortuous, distorted and considerably lengthened. The mucosa was of a uniform deep red, dotted over with numerous blue puncta, indicating the terminal points of the arterial branches. The thickness and consistency of the mucosa, so far as macroscopical appearances were concerned, were normal, and in only one area on the lateral wall of the fundus was there any encroachment of the interstitial tumors upon the cavity, and even here the small nodule, although projecting as a hillock into the fundus, had as yet induced no mechanical changes in the endometrium. The partially subperitoneal tumors are as yet well provided with a peripheral wreath of vessels, although the substance is of an alabaster-like whiteness.

Epitome of observations.—Usual circulatory phenomena resulting from the injection of one artery; tumors all interstitial, some moving toward the peritoneum while one small one tends to become submucous; mucosa intact, no mechanical changes.

Remarks.—In this case the patient entered the Hospital suffering from the effects of chronic salpingitis and peri-öophoritis, the lateral structures being intensely adherent and extensively diseased. The operation of total extirpation was therefore

indicated, not for the relief of the myomatous condition, but for the lateral disease. Given such a case as this, without any coincident disease of the appendages, the proper treatment should be absolutely conservative, for there is no immediate indication for operation. Should, however, the menses become too profuse or irregular a simple curettage would suffice to relieve the symptom, for we see that at this stage of growth there is but the one small tumor tending to become submucous, while the others push out towards the peritoneum. Such cases as these may go on to the formation of multinodular pedunculated submucous tumors, which sooner or later undergo softening and expulsion, after which all uncomfortable symptoms cease.

Case IV. *Menstrual history.*—Flow began at 16 years, at first monthly, but during the last six years her periods have been two months apart. Flow continues one week, then ceases for 1½ days to return for 2 or 3 days. Flow is scant and accompanied by pain. Last period May 2d. Operation May 9th.

Description of specimen.—Globular myoma, measuring 15x10 cm., occupying the posterior wall of the uterus.

Injection.—Carmine gelatine. At the completion of the injection the red gelatine was escaping in a small filmy stream from the cervix.

Examination of specimen.—On section the tumor presented on first sight all of the appearances of the submucous variety, but on closer inspection was found to be entirely interstitial, for although projecting very greatly into the uterine cavity it was nevertheless surrounded entirely by the uterine musculature, which averaged 1 cm. in thickness. The mucosa was not perceptibly thinned out. The tumor itself, contrary to the usual rule, was extremely vascular, being penetrated by many large dilated vessels.

In the uterine tissue between the myoma and the mucosa there were many large vessels, which in the mobilization of the tumor had been pushed ahead of it. The tumor projected 6 cm. into the uterine cavity, having originated in the fundal portion and grown downward into the cavity, distending it quite equably on all sides. The endometrium was intact and showed no thinning at any point, except at the apex of the tumor, where it was slightly atrophic.

Epitome of observations.—Single large interstitial globular tumors which, so far as morphology was concerned, presented at first sight the appearance of a submucous tumor. Marked exception to the rule on account of extreme vascularity of tumor. Little or no atrophy of mucosa. No excessive bleeding, on the contrary decrease in the frequency of the menstrual periods.

Remarks.—This is one of the most interesting cases in my entire collection, because it illustrates so well the purely mechanical principles governing the deviation of the menses from the normal flow. Here, notwithstanding the excessive vascularity of the tumor and the uterine wall, the patient had suffered from absolutely no excess in her menstrual bleeding. The study of the specimen at once shows that the two essentials for hemorrhage, first, the erosion of the mucosa and second the retardation or stagnation of the blood currents through the mechanical conditions induced by the tumor, are absent, consequently no hemorrhage had occurred. The second point to which I would draw attention are the possibilities in the line of operation. Although this tumor was quite large and had caused wide distention of the uterine wall and extensive distortion of the uterine cavity, a simple myomectomy could nevertheless have been performed, leaving to this woman, who was only 36 years of age, a uterus which might sooner or later have been sufficiently restored to its normal shape and condition as to be capable of bearing a child. A simple myomectomy is now invariably performed upon such cases in the gynecological clinic of the Johns Hopkins Hospital without even the thought of resorting to hysterectomy.

Case V. *Menstrual history.*—Menses at 13; as a rule regular, painless, duration 5 to 7 days. Of late the flow has grown more profuse, but is still regular.

Description of specimen.—Large globular uterus 6x16 cm. in size with densely adherent and mutilated left ovary and tube. The consistency of the tumor is soft, doughy and plastic, and can be moulded into any shape.

The main development of the tumor is in the posterior wall of the uterus and partakes of the characteristics of both the submucous and subperitoneal types on account of its growth towards the peritoneal and uterine cavities.

Injection.—Carmine gelatine. Points of injection, the left uterine and right ovarian vessels. The first point injected was the uterine vessel from which the left lower segment was first colored red, then the left cornu and middle portion, following which the injection mass rapidly spread over the entire uterus, imparting a brilliant carmine red color to it.

To insure the fullest distention of the vessels, notwithstanding the apparent perfect injection of the entire circulatory system, fluid was forced into the right ovarian vessel. During the course of the injection the red gelatine, as in other preceding experiments, began to escape from the cervical canal.

Examination of specimen.—On opening the uterus the tumor was found to be a large interstitial one, undergoing necrosis. The peritoneal covering and capsule of the myoma showed a uniform intense red and blue injection, but at the point where it presented towards the uterine cavity was especially rich in vessels. The uterine cavity was considerably lengthened but not distorted. The endometrium was of a deep carmine color with numerous blue points appearing quite uniformly over its surface. The tumor itself was necrotic, its center consisting of a soft pulpy mass. The study of the injected fields in connection with the necrotic process is interesting, but offers no novel observation. As would be expected, the areas in which the circulation has been retarded, or has ceased altogether, are the ones undergoing necrosis.

The posterior portion of the tumor, next to the uterine cavity, is poorly vascularized, but near the apex two muscular whirls are still preserved which contain a few injected vessels. The central necrotic area shows no trace of blood-vessels.

The capsule of the tumor at its apex is one-half cm., in the anterior wall 2 cm., between the uterine cornu 1 cm., and opposite the uterine cavity 1 cm. in thickness.

The uterine mucosa is intact and at no point is attenuated.

In this case the vessels of the capsule between the mucosa and uterine cavity were quite large and dilated.

Epitome of observations.—Large intramural myoma undergoing necrosis, vascular system within tumor almost completely destroyed, no involvement of uterine mucosa. Menstrual bleeding increased but no inter-menstrual flow.

Remarks.—In such a case as this the question naturally arises, What are the chances for final absorption of the tumor? With such a rich vascular supply around the tumor and its isolation from the uterine cavity the probabilities are that in time it would have entirely disappeared. The retrogressive changes, however, might have been slow, and the symptoms attending the absorptive process so unpleasant that we cannot consider this a case for conservative treatment, especially in view of the fact that the woman was 42 years old at the time of her admission to the Hospital. This case is a good illustration of that type so frequently referred to in medical literature in which the tumor disappears at or about the menopause. That this occurrence, however, is not of sufficient certainty to be depended upon will be shown in the reports of cases from the Johns Hopkins Hospital, for according to our observations the menopause is quite likely to be much slower in appearing, and even then the tumor instead of decreasing may grow larger.

I can hardly think it possible in such a case as this to achieve much success with a conservative operation; on the contrary, I should consider it bad surgery to attempt to save a useless organ in a woman 42 years of age, especially if this attempt were to be attended with more danger than a simple hysterectomy.

CASE VI. *Menstrual history.*—Flow began at 14 years; regular until 3 years ago; since then irregular, occurring some months twice and then possibly not for two months or more. Flow not excessive, lasting 4 days.

Description of specimen.—The specimen consists of a myomatous uterus and the right ovary and tube. The uterus is irregular in shape, being distended in its right latero-posterior walls by a globular intramural myoma 4x4 cm. in size. With this exception the general form of the uterus is preserved, measuring 7 cm. in length by 8 cm. in greatest width. Length of uterine cavity 5 cm.

Tube and ovary have been densely adherent, and are more or less mutilated by the operation.

Injection.—Carmine and granular ultramarine blue gelatine. Only a very slight amount of the red fluid oozed from the uterine cavity during the injection.

Examination of specimen.—Section through the center of uterus shows the uterine cavity and the endometrium to be normal.

The myoma, which occupies one lateral wall, is strictly intramural and does not impinge upon the uterine mucosa. The tumor itself is sparsely vascularized, but has a very rich aggregation of vessels surrounding it.

Remarks.—In this case the indication for operation was the diseased condition of the ovaries and tubes, the myoma being merely a coincident complication.

In a case like this, unassociated with any pathological condition of the appendages, the line of treatment should be absolutely conservative, for a tumor of this nature gives no discomfort until it has increased very markedly in size. With a simple growth like this, in which there is no impingement upon the mucosa, no derangement of function as a rule occurs. The slight change in the periodicity of the menses noted in the menstrual history can be accounted for much more readily by the diseased condition of the appendage than through any influence exerted by the myoma.

CASE VII. *Menstrual history.* Until a few months ago flow has been profuse, but not irregular; since then it has, at times, been almost constant.

Description of specimen.—Specimen consists of a uterus very greatly distorted by three myomata, one 7x7 cm. in size, occupying the fundus; the other two (5x5x4 cm. in size) the lateral walls of the uterus.

Injection.—Carmine and granular blue gelatines. At the completion of the injection the red fluid was running from the uterus in quite a stream.

Examination of specimen.—Section through the nodule in the fundus shows it to be poorly vascularized while the surrounding uterine muscle presents a uniform red color with numerous blue points, indicating the position of the arteries. The tumor pushes down into the uterine cavity and is more than half submucous. The endometrium over the tumor has almost entirely disappeared, leaving the tumor towards its apex with a glazed whitish appearance and covered by thin-walled exposed vessels.

The mucosa is intact at the base of the tumor, but as it extends downward gradually becomes thinner and thinner until it reaches an equatorial zone or line of demarcation, where it is completely eroded and the vessels appear upon the surface. From the appearance of the vessels they are without doubt the original vessels which have surrounded the tumor in its intramural state, and with its mobilization towards the uterine cavity, have been pushed ahead of it. A small submucous tumor just below this one shows the same characteristics. A third submucous tumor springing from the lateral wall, through contact with the large tumor has been deeply indented. The mucosa of that portion of the uterine cavity not impinged upon by the submucous tumors appears considerably heaped up and thickened.

The two interstitial nodules show a moderately good injection, but not so intense as that of the surrounding uterine muscle.

Epitome of observations.—Large submucous tumor, the vessels of the capsule of which have become exposed by erosion and have given rise to profuse hemorrhage through rupture and diapedesis. Two interstitial tumors showing the typical wreath-like arrangement of their external vessels and a relatively poor internal vascularization.

Remarks.—This case shows best of all the mechanical basis for the excessive hemorrhage in advanced types of submucous myomata. Observations made in preceding cases taken in conjunction with the evident conclusions which may be drawn from the case in hand permits us with little doubt to outline the progress and the attendant symptoms of the submucous tumor distending the uterine cavity. At first it has originated as an interstitial tumor, with a rich peripheral blood supply like those which still occupy an intramural position, but

through a disturbance of the surrounding equilibrium, excited by the contraction of the uterine muscle, it has begun to move towards the uterine cavity, that being, in this particular instance, the line of least resistance.

In its progress it has carried its surrounding wreath of vessels until the endometrium has been reached, and this, through the excessive tension produced by the tumor, has become attenuated and finally eroded until the capsule of the tumor, with its large thin-walled vessels, were exposed.

As resultant symptoms of the mobilization of this tumor, there was first an increased menstrual flow, due simply to congestion and stasis, but later through attenuation of the endometrium and exposure of its vessels; this became excessive and finally when the large sinus-like vessels became exposed, any slight exertion, such as undue exercise, coitus, etc., would give rise to profuse inter-menstrual hemorrhages simply through excessive diapedesis and actual rupture of the vessels.

While the mucosa in the areas covering the myomata was undergoing erosion that of the remaining portion of the cavity was being heaped up and increased in thickness, not only by a mere mechanical crowding and sliding upon its muscular base, but also through an actual hypertrophy or through congestion and oedema.

It is needless to say that any course of treatment in this case short of hysterectomy would be questionable, for the excessive involvement and great increase in the volume of the uterus with the marked distortion of the cavity would leave little hope of preserving the organ, even in the hands of the most skilled plastic surgeon.

Case VIII.* *Menstrual history.*—No derangement of flow. *Description of specimen.*—The uterus is converted into a large irregular mass 21x18 cm. in size, consisting of one large subperitoneal tumor measuring 5x6 cm., several small ones of the same variety, and numerous palpable interstitial tumors.

The large subperitoneal tumor has become pedunculated, and although the blood supply, carried through the thick, fleshy pedicle would appear to be sufficient to maintain the nutrition of the myoma, it has secured an additional source, having established an adventitious or parasitic communication with the vessels of the left ovary, from the inner pole of which a large congeries of vessels cross over through a bridge of adhesions and spread out upon the apex of the tumor.

Injection.—Liquid Prussian blue with cinnabar granules held in suspension by agitation. The left ovarian artery was first injected, the vessels of the broad ligament and the ovary first took the coloring matter, and then the fluid was seen to pass over the bridge of adhesions and penetrate the apex of the tumor. In the meantime the uterine branch of the ovarian artery had quickly carried the fluid to the uterus and almost simultaneously with the appearance in the tumor of the blue color from the adventitious vessels, it was also beginning to show itself in the pedicle and base of the tumor. About this time the cannula became blocked and the simple blue solution was then forced into the opposite ovarian artery, when the tumor and the remainder of the uterus assumed a deep blue color.

Examination of specimen.—On bisection of the tumor mass it was found that the large subperitoneal myoma, notwithstanding its adventitious and ordinary blood supplies, was undergoing necrosis, the center having already been converted into a pulpy mass. The other subperitoneal and two or more of the interstitial growths also showed a very poor vascularization.

The uterine cavity occupied a median position between the many tumors and, although distorted, at no point was there any invasion by the interstitial tumors.

The mucosa in general was thin but appeared perfectly normal with the exception of an area where a slight erosion had occurred.

At this spot evidences of a recent hemorrhage were seen.

Epitome of observation.—Subperitoneal myoma which, notwithstanding a second or adventitious blood supply had undergone necrosis. Little involvement of the endometrium. Tumors numerous, but all interstitial or subperitoneal.

Remarks.—This case represents the type of parasitic tumors which are by no means uncommon within the abdomen.

As a rule, the most common adventitious vascular source in such instances is the omentum. Frequently the nutrition of myomata, dermoid and simple ovarian cysts is greatly increased by the penetration of the growth with vessels from the omentum. Indeed it is not uncommon for tumors to maintain an existence even after a total severance from their original blood supply.

From our present operative standpoint in this case, only the radical operation could be advised, as it can readily be appreciated, that it admitted of no conservative treatment.

Note.—The reader's attention is called to a colored plate in Kelly's *Operative Gynecology*, Vol. II, p. 338, Plate XIX, drawn from a case in my series of injected specimens showing all the types of tumors. The relatively poor vascularization of the tumors stands in marked contrast to the deep carmine red of the uterine musculature. The main source of hemorrhage in the submucous variety is indicated by the vascular halo around the projecting tumor.

* On account of similarity to other cases in this report, Cases IX and X have been omitted.

A STUDY OF SIXTY-SEVEN CASES OF PRIMARY MALIGNANT TUMORS OF THE SUPRARENAL GLAND.

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Primary malignant tumors of the suprarenal gland are among the rarer forms of abdominal new-growths, and it is probably for this reason that so little attention has been paid to them in medical literature. Now, however, as sureness in diagnosis increases and as abdominal surgery is becoming daily more simple and less dangerous, it seems time that a more prominent place should be given them in the roster of abdominal tumors.

I have endeavored, as far as possible, to collect all the published cases, and from them and the three which I have seen personally, to draw some conclusions as to the symptoms, the prognosis and the possibilities of operative treatment. No attempt has been made to discuss at any length the etiology of these growths, as it would involve too much space and be merely a reiteration of views already published.

Many difficulties have been encountered in this task, chiefly due to the incompleteness of the reports, and I have not attempted to change the classification of the tumors and have tabulated them under the name by which they were described by the author, though I was struck with the number of carcinomata observed by the older writers as compared with those seen at the present time.

The first two cases were admitted to the Gynæcological Department of the Johns Hopkins Hospital, and were operated upon by Dr. Howard A. Kelly. The third case, which was operated upon in the Surgical Department, I owe to the courtesy of Dr. J. M. T. Finney.

CASE I.—*Globular Tumor in the Right Renal Region. Operation. Recovery.*

Mrs. C., white, age 53, was admitted to the Gynæcological Ward of the Johns Hopkins Hospital, Dec. 26, 1896, complaining of a tumor in the right side of the abdomen. Her family history was good.

She has had the usual diseases of childhood, but otherwise has always been a healthy woman. Eight years before a cystic tumor of the right breast was removed. She had always menstruated irregularly, the menopause occurring at the age of 50. In January, 1895, or just one year before the patient was admitted to the Hospital, she first noticed a small, hard, oblong mass in the right side of the abdomen, which has slowly increased in size up to the present time accompanied by continuous stinging pain in the right lower abdomen, which has been much more severe during the past three weeks. The abdomen has never been distended, and she has never had any jaundice. She has lost 20 pounds in the last three weeks, is thin and anæmic in appearance, and there is a very slight brownish discoloration of the skin in places. The patient has never noticed any discoloration of the urine by blood, and on several careful urinary examinations after her admission to the Hospital no blood could be detected. The bowels have always been constipated.

On examination, the right side of the abdomen is found to be the seat of a large globular tumor, which occupies chiefly the right hypochondriac, the right side of the epigastric, and the upper portion of the umbilical regions, and the right flank below the ribs is bulged out by this tumor. On respiration the skin is seen to move over the tumor, but there is no respiratory movement of the tumor itself. On palpation a globular mass is felt, occupying the right side of the abdomen and reaching to the middle line. Above, the border is not distinct, but a deep furrow separates it from the costal margin. The most prominent portion anteriorly is occupied by a hard, rounded ridge extending inward and slightly downward, the ridge being about 12 cm. in length and 4 cm. in breadth, the ends appearing gradually to merge into the tumor. The surface except for this ridge and several smaller rounded prominences is smooth. It is slightly movable towards the left to firm pressure but gives the feeling of a fixed tumor. The measurement from above downward is 6½ inches, the greatest diameter being oblique, from the external border downward and inward—this measurement being 7 inches. The percussion note over the tumor is only slightly tympanitic in quality, save over the lower inner portion, where tympanitic resonance is found.

The clinical diagnosis of a renal new-growth was made from the position of the tumor, the history of constant increase in its size, and in spite of blood never having been found in the urine. It must be stated that a tumor of the suprarenal capsule or other retroperitoneal growth in this situation was never for a moment considered, notwithstanding the presence of the rounded ridge, so like in shape and size to a kidney.

Operation.—An incision was made in the median line 12 cm. in length. On opening the abdominal cavity the tumor was found generally adherent and crossed on the lower portion by the colon; the prominent ridge above spoken of was found to be the right kidney displaced and lying in front of the tumor. The peritoneum was carefully stripped off on both sides, the operator working down towards the vessels lying under the tumor. The ureter was first recognized and cut between two ligatures. The tumor was then somewhat raised, and first the large renal vein and then the artery were caught and tied, these maneuvers being difficult because of the proximity of vena cava. An enlarged gland near the upper portion was removed with the tumor. After the tumor was removed a counter-opening was made in the lumbar region and a gauze drain inserted.

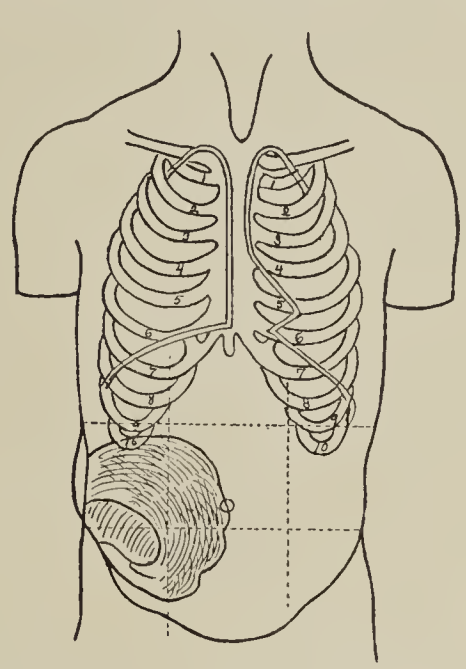


FIG. 1.—Shape and position of tumor. The rounded body indicated was the misplaced kidney.

The convalescence was retarded during the first three days by nausea and profuse vomiting, the vomitus being a brownish fluid. The pulse during the first few days was rapid and weak. The bowels were well moved on the fourth day, and after this the convalescence was uncomplicated.

The urine during the first day after operation measured 260+cc., the plus mark standing for an unknown amount which was lost; on the second day 625 cc., on the third day 275+cc., and on the fourth day 620 cc.

In a note made just before her discharge from the Hospital the slight brownish discoloration of the skin was noted as disappearing.

Pathological Examination of the Specimen Removed.—The specimen consists of the right kidney and a large retroperitoneal tumor. The tumor is irregularly globular in shape, measuring 11x11x13 cm., and presents a somewhat lobulated appearance, the larger nodules, which are three or four in number, averaging 3 or 4 cm. in diameter and projecting 1 or 2 cm. above the general surface of the tumor. One springing from the upper posterior portion is firm and resistant to the touch, the remaining nodules and the large tumor are distinctly fluctuant. The tumor is entirely enveloped in a vascular capsule with large and abundant vessels ramifying

through it, and where this is stripped off the tumor is of a yellowish color. Situated on the anterior surface of the tumor and attached to it by the lower four-fifths of its posterior surface by connective tissue is the slightly enlarged kidney, measuring 13x7x3.5 cm. The kidney for the most part has a deep red, mottled appearance, but presents a few bands or small areas of whitish fibrous tissue, and the upper portion of the anterior surface is occupied by an oval area 5.5 x 3 cm., which is of a yellowish-white color and slightly raised above the surrounding tissue.

Surrounding the tumor is a large amount of adipose tissue, and on the upper end of the kidney is a conical body 2.3 cm. long, firm to the touch and probably an enlarged lymph gland. Originating from the junction of the upper and middle thirds of the anterior margin of the kidney and crossing over the anterior convexity of the tumor is the flattened ureter resembling an empty vein.

After hardening in Müller's fluid and alcohol a cross-section through the kidney and tumor was made, dividing it into two equal halves, and it was then found that it was a thick-walled cyst, the walls measuring from 1 to 7 cm. in thickness, and the contents a thick yellowish colloid material. In several places in the wall, especially in the thicker portions which represented the bosses above spoken of, there were irregular cyst-like cavities containing the same colloid material. Sections made through various portions of the wall were studied microscopically and the following characteristics were seen. The cyst cavity had no definite limiting membrane, it being bounded by a layer of connective tissue poor in cell nuclei. Deeper in the tissue the character of the wall changed entirely. Here were found cells varying greatly in size and shape, some round, spindle, or irregularly shaped, and with round or oval rather lightly staining nuclei, with here and there a larger cell containing from 3 to 7 nuclei. These groups of cells were crossed in places by bands of lightly staining tissue. In other places again typical myxomatous tissue was found, and scattered through the wall were areas of connective tissue, which in places showed hyaline changes, and in others were thickly set with numerous small round cells, with round deeply staining nuclei. The tissue showed in places quite a number of blood-vessels, some being apparently formed of the tissue cells, while in other parts of the section the blood-supply is very poor, and this was specially noted where the hyaline changes were most marked. No suprarenal tissue was found in any of the sections.

The examination of the enlarged gland showed no metastasis, there being merely a hyperplasia of the tissue, which in places showed marked hyaline degeneration and commencing calcification. The kidney also showed no evidences of metastases ; the whitish area above spoken of was due to a great increase in the interstitial connective tissue, with loss of the epithelium of the tubules and glomeruli, probably the result of interference with the blood-supply.

Diagnosis.—Fibro-myxo-sarcoma of the right suprarenal gland.

Case II.—*Large Tumor in the Left Renal Region. Operation. Death.*

Mrs. C., white, aged 64, was admitted to the Johns Hopkins Hospital, February 11, 1897, complaining of a "lump" in the left side of the abdomen.

Her family history has always been good, and she has been a healthy woman, save for puerperal fever, which followed the birth of her child. The climacteric period appeared unusually early, menstruation ceasing entirely when she was but 30 years old. One year before her admission she began to feel badly, but complained of no definite illness. Two months ago she first noticed a tumor in the right side of the abdomen, about the size, at that time, of a goose egg, but which has since then grown rapidly, though without pain of any kind. She has lost flesh rapidly of late and feels weak and exhausted. The bowels have been obstinately constipated, and she complains of a sense of obstruction in the rectum. The urine never showed any signs of blood, and careful urinary examination, made after her entrance into the Hospital, showed a complete absence of blood from the urine.

The temperature taken twice daily for a week, between the time of entrance into the Hospital and the operation, was normal, only twice being found above 99°. There were no subnormal drops in the temperature. No brownish discoloration of the skin.

Physical Examination.—On inspection, a large rounded tumor can be seen filling the whole of the left side of the abdomen, with marked bulging of left flank below the ribs. There is no movement of the tumor with respiration. On palpation the tumor is found to be rounded, and no sharp edge can be felt. The surface is smooth, and the tumor has an elastic, almost fluctuant feel. It extends from just below the costal margin above, nearly to the level of the anterior superior spine below, and inward nearly to the median line. In its transverse diameter the tumor measures 20 cm. and measures 19 cm. from above downward. It is not tender on palpation, and is almost immovable, though with firm pressure it can be pushed slightly towards the median line. On percussion there is dull tympany over the lower inner portion, and here gurgling can be felt on palpation. The border of the liver can be palpated 2½ inches below the costal margin, and on pressure there is a sense of resistance and pain in the epigastric region.

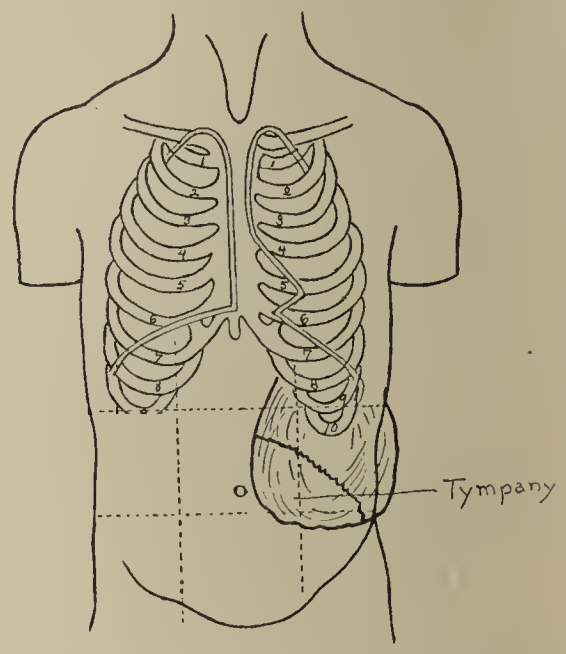


Fig. 2.—Shows position of tumor; the dark line is drawn to indicate where the tympanitic note ended.

The clinical diagnosis was "renal tumor" probably sarcoma from the rapid growth and elastic semifluctuant feel, though in this case, also, blood had never been found in the urine.

Operation.—The incision was made over the most prominent portion of the mass, beginning at the left linea semilunaris, on a level with the umbilicus, and extending around to the quadratus lumborum muscle, the incision measuring 25 cm. in length.

On opening the peritoneal cavity a large tumor was found occupying the left renal region, the surface being covered with extremely large veins. The kidney was displaced below and slightly behind the tumor, making it impossible to palpate it during the physical examination. The peritoneum was incised and pressed off the tumor by blunt dissection. Several large veins were cut and tied, but a great deal of blood was lost while attempting to free the tumor enough to reach the vessels below. By careful dissection, however, the tumor was partly raised from its bed, when on using a little more force than necessary the capsule ruptured, and masses of a soft tissue, looking like brain substance, poured out of the rent, accompanied by free hæmorrhage. After this the attempt to remove the tumor completely was given up, the principal masses being taken

out piece-meal, one portion of the tumor being removed with the kidney. The vessels were tied, and after washing out much of the detritus with hot salt solution, a drain was introduced and the wound closed. On removing the patient from the operating table, no pulse could be felt at the wrist, and the face and extremities were cold and clammy. On her return to the ward, the foot of the bed was raised, stimulants were freely given hypodermically, and 1000 cc. of salt solution were infused under the breasts, while the arms and legs were bandaged. In spite of this however, she never recovered consciousness, and died one hour after leaving the operating room.

No autopsy was permitted, so we were unable to settle the question of metastases.

Pathological Examination of the Tissues Removed.—The specimen consists of a left kidney and a large tumor mass, weighing together 2340 grams. The tumor was mutilated during the operation, and consists of several large masses, to one of which the kidney was attached by its anterior surface. The tumor consists of a thin membranous sac, in many places less than 1 mm. in thickness. Springing from the inner surface of the sac and forming the contents of the tumor are masses of exceedingly friable tissue which, where the degeneration is not too far advanced, present a fine papillary or thread-like structure. On section of some of the larger masses they are found to consist of a fibrillated, apparently myxomatous tissue, enclosing irregular masses of a soft brain-like substance. The surface of the tumor is covered by dense adhesions.

The kidney measures 13x5.5x5; its surface is irregularly nodular, the fœtal lobulations being well marked; the color is bluish or reddish. The lobules are in part firm and resistant, representing the fœtal lobulations; in other places they consist of thin-walled cysts, varying from 3 mm. to 2.5 cm. in diameter. Emerging from the upper and lower angles of the hilum are two ureters, and several large arteries are present in the hilum.

Microscopically, the thin membranous sac is found to be composed of connective tissue, with a few elastic fibres scattered through it; from its inner surface there are numerous bands of connective tissue extending inward toward the center of the growth, and in the meshes thus formed are found cells, varying greatly in size and shape, some being oval, some round and some very irregular. The nuclei of these cells are usually round or oval, though in places they are very irregular and stain deeply. Sections cut from the centre of the growth show the same characteristic structure, there being thick bands of connective tissue extending in various directions through the growth, and from these thick bands smaller bands are given, dividing the groups of cells, which in some places are packed in closely, and in others almost every cell is separated by a fine connective tissue fibril from the others; again, in other places, though the meshes are quite good size, only a few irregularly shaped cells are found in it.

The blood-vessels follow chiefly the bands of connective tissue, though in places one can see among the cells blood enclosed either by one layer of flat cells, or in some cases apparently limited by the tumor tissue.

The kidney showed metastatic growth, following closely in type the primary tumor.

Diagnosis.—Large, round-celled alveolar sarcoma.

CASE III.—*Globular Tumor in the Left Renal Region. Operation. Death.*

Mr. M., white, æt. 53, was admitted to the Medical Ward of the Johns Hopkins Hospital, June 18, 1896, complaining of the presence of a tumor in the right side of the abdomen. The patient has had the usual diseases of childhood but otherwise considered himself a healthy man, and denied any venereal infection. In January, 1896, or six months before his admission to the Hospital he suffered with an attack of severe pain in the left side, which his physician thought due to impaction of fæces and which was relieved by simple purgation, but after the pain had disappeared a lump was discovered in the same side of the abdomen, which never disappeared. Since then the patient has never had an acute attack like the first but has complained at times of some soreness localized in the left side and never radiating. The bowels have always been regular. The stools have never contained blood or mucus, and he has never vomited, nor showed any signs of jaundice. During the six months he has lost 20 pounds in weight and becomes very easily exhausted on any exertion. The urine has always been light in color and normal in quantity. The clinical and microscopical examinations of the urine revealed nothing abnormal.

Examination shows the patient to be a healthy-looking man, though there is a fairly well marked cachexia. The heart and lungs are normal. In the left hypochondrium extending into the epigastrium there is a prominence which fills the costal groove. On palpation, corresponding to this area, there is a firm mass occupying the left half of the epigastrium. The mass does not extend much beyond the middle line. Below, it slopes gradually and passes deeply into the posterior portion of the abdominal cavity. The deepest point can be felt almost on a level with the umbilicus.

Along the costal margin it can be felt passing deeply and filling in the upper part of the space between the costal margin and the iliac crest. Fingers in the renal region behind push the mass forward, though it is difficult to outline at times by bimanua palpation, and there is some tenderness on palpation.

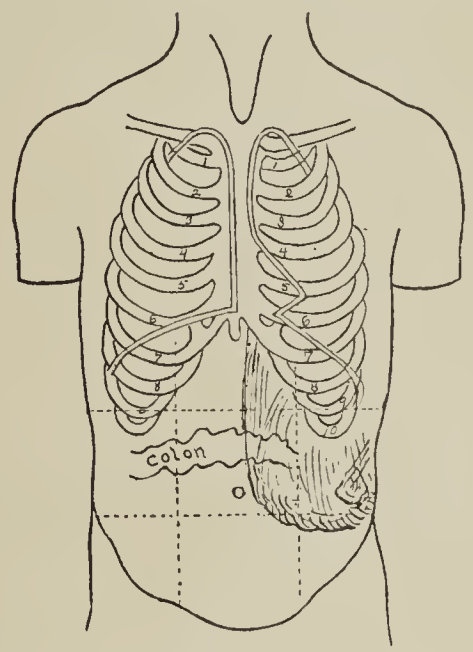


FIG. 3.—Shows position of tumor. Transverse colon, crossed inner portion.

The surface of the tumor is somewhat nodular in the flank and one nodular mass can be felt low down in the flank below the level of the umbilicus. Crossing the tumor transversely there is a large sausage-shaped mass, probably the colon.

After a week the patient was transferred to the Surgical Division and operated on by Dr. J. M. T. Finney, June 30, 1896.

Operation.—A transverse incision was made below the costal margin on the left side. The tumor was found to be quite adherent and was removed with difficulty, though there was no very marked hæmorrhage, and the tumor was not broken up during the removal. It was doubtful for a time from which organ the tumor sprang, and it was at first considered to take origin from the left kidney. This was found intact and was left behind during the removal of the tumor. The spleen was pushed high up under the diaphragm, and on studying the relations of the tumor more closely, especially its relations to the kidney, it was found to be undoubtedly supra-

renal in character. As the patient was in a bad condition no further search was made, and the wound was closed.

Death occurred at 2.45 A. M., about twelve hours after the operation, from shock.

Pathological Examination of the Specimen Removed.—The tumor is an irregularly round mass about the size of a child's head, hard and firm in consistence over most of its area, but on the anterior surface there are several soft cystic elevations, each about the size of an English walnut. On opening one of these a soft brownish material characteristic of sarcoma exudes, and through the opening a probe could be passed well into the centre of the growth.

Microscopical Examination.—The capsule is of dense fibrous tissue, with distinct areas of round-cell infiltration in places. The cells lying immediately beneath the capsule are irregular in shape and vary greatly in size, some large and oval, with irregular nuclei, others round, and others again almost spindle-shaped. Numerous connective-tissue bands divide the cells up into groups, and in several places the individual cells are seen separated by fine connective-tissue fibres. This alveolar arrangement can be seen in many places, some of the alveoli being filled with the irregular cells, while in others the cells are principally distributed around the edges.

In another portion of the tumor many small blood-vessels are seen surrounded by denser masses of cells, which apparently take origin from the small blood-vessels and suggest in their arrangement a perithelioma. Giant cells are found in several portions of the tumor, usually with many centrally placed nuclei, and a protoplasm, granular, and staining deeply with eosin, and there is also a small area in another portion of the tumor which looks like normal suprarenal gland tissue.

Diagnosis.—Alveolar sarcoma of suprarenal gland.

The histogenesis of these tumors is still a matter of discussion, and many observations have appeared on the subject chiefly in connection with the new-growths in the kidney, taking origin from aberrant suprarenal tissue. Upon this point very little of added importance can be obtained from my specimens.

One interesting thing, however, was noted in the microscopical examination of sections from the tumor in Case III. In this many of the smaller blood-vessels were found surrounded by dense groups of cells, which apparently took origin from the endothelial cells of the vessel wall, and the tumor might therefore be classed as a perithelioma, though I have considered it as an alveolar sarcoma, for the principal picture was of a tumor of this type.

The ages of patients affected varied widely, and in the sixty-seven cases comprising both the carcinomata and sarcomata, the youngest was only 9 months old, while the oldest was 73 years.

Out of 37 cases of carcinoma, 22 occurred in the male and 15 in the female sex. Mankiewicz,[51] from the statistics which he gathered, considered carcinoma more common in the male sex, he having found 7 cases in the male to 4 in the female, and my statistics bear out this view, though from the limited number very little dependence can be placed on the figures. The average age in the 37 cases was 43.4 years, the youngest patient being 3 years old, the oldest 73 years old, and both the youngest and oldest being females.

Table I shows in which decades the carcinomata occur most frequently:

Table I.

Age not given	=2
1 year to 20 years	=5
20 " " 30 "	=3
30 " " 40 "	=7
40 " " 50 "	=5
50 " " 60 "	=8
60 " " 70 "	=6
70 " " 80 "	=1

The averages for the sarcomata were drawn from 30 cases, of which 14 occurred in the male and 11 in the female, the sex of five not being noted. In this group the preponderance of the male over the female sex is not so marked. The average age of the 30 cases was 31 years, the youngest being 6 months old, the oldest 64 years.

Table II shows the relative frequency of occurrence in the various decades of life:

Table II.

6 months to 10 years	=8
10 years " 20 "	=1
20 " " 30 "	=2
30 " " 40 "	=2
40 " " 50 "	=7 (?)
50 " " 60 "	=4
60 " " 70 "	=2

I am sure that the above figures are not of much value in making the diagnosis between carcinoma and sarcoma, as some of the tumors classified as carcinomata were undoubtedly sarcomata, and probably vice versa, but they show that the male sex is more frequently attacked than the female.

Symptoms.

In first studying the symptoms connected with a suprarenal neoplasm, a resemblance to the classical description of Addison's disease is immediately seen. This resemblance was first noticed by Addison himself while studying the disease which has received his name, and in his monograph[1] he speaks of two cases of secondary carcinoma of the suprarenal gland in both of which many of the symptoms were similar to those occurring in tuberculosis of the gland, and though the skin did not show the typical bronzing there was a peculiar dirty brownish color present, which, since then, has been noted by other observers as occurring in the new-growths of the suprarenal gland. From these two cases Addison classified malignant neoplasms of the suprarenal as one of the causes of Addison's disease.

On considering, however, more carefully the symptoms complained of in the cases collected, and in comparing them with the definition given by Addison, the resemblance is not nearly so marked, and especially the skin changes and the disturbances of the circulatory system are absent in most of our cases.

I will not attempt the question as to whether in Addison's disease, and of course also in other disturbance or destruction of suprarenal capsule, the symptoms, more especially the skin changes, are due to changes in the suprarenal itself, or to

involvement of the sympathetic nervous system, but will merely quote several interesting cases, as tending to prove that some of the symptoms may be due to involvement of the sympathetic fibres, rather than to changes in the suprarenal gland. Fleiner[64] described a case of primary carcinoma of the stomach with metastases to various abdominal organs, among them the suprarenal glands. There was a distinct bronzing of the skin and of the mucous membrane of the mouth, and besides the carcinoma of the suprarenal there was a carcinomatous involvement of the abdominal sympathetic nerves. Leva[19] describes two cases of primary suprarenal new-growth without pigmentation, in which the abdominal sympathetic nerves were not involved, and explains the common absence of bronzing in this affection by the idea that the bronzing is due rather to involvement of the sympathetic nerves than to changes in the suprarenal gland, and he thinks tuberculosis is much more apt to involve the sympathetics, and therefore, more apt to cause the bronzing.

The case of Fleiner seems to bear out Leva's theory quite well, and it seems rather strange, to say the least, that if the pigmentation is due to destruction of the gland alone why we should not always see it in malignant growths.

In the attempt to classify the symptoms, carelessness in reporting cases gave much trouble; I found also a certain number of cases in which the symptoms given were evidently due to other diseases, which were either the actual cause of death, or which were so marked as to mask the suprarenal symptoms.

In the 67 cases collected there were only 37 which could be used in studying the symptoms. In these, the following symptoms were seen, cited in the order of frequency.

The most frequent symptom, seen in 22 patients, was a marked and steadily increasing loss of strength, accompanied in many cases by extreme languor and debility. Affleck and Leith[36] call especial attention to this languor in a case which they report, and say that "the difficulty of arriving at any diagnosis was enhanced by the natural apathy and indifference of the patient, due, no doubt, to the disease." Emaciation varying greatly in degree was noted in 20 cases; in some of these the loss of flesh was apparently not very marked, though in a few it was noted as extreme.

The intestinal system was the next attacked, in point of frequency: twelve patients out of 37 complained of nausea and vomiting. In nine there was loss of appetite; in four, diarrhœa; and in five, constipation. The circulatory system as compared to Addison's disease was rarely involved: four patients complained of palpitation of the heart, and in one the pulse was weak and thready. Six suffered with œdema of the legs, due in most of the cases at least to renal changes and not connected with the new-growth. Anæmia, varying from slight pallor to a high grade, was noted in seven cases.

Of interest is the fact that though there was extension of the growth into the vena cava and thrombosis, in four or five cases, these did not suffer with œdema. Affleck and Leith[36] call attention to this fact, and explain it by the collateral circulation which is established.

Complaint of pain located in various parts of the body was made in 25 cases. In some it was found in one or the other renal regions behind; again it occupied the whole back, extending upwards into the shoulders, or downward into the thighs; others again complained of pain in the epigastrium or in one or the other hypochondriac regions; and in several there was marked tenderness on pressure either in the epigastrium or over the tumor. The pain was usually of an intermittent character when present, though occasionally it was continuous. In one case there was such severe pain in the knee and ankle joints that the medical attendant considered the patient to be suffering with rheumatism.

The skin changes were usually not marked; three out of the 37 showed distinct bronzing of the skin, and in nine there was some change in the color or texture of the skin, as for instance several patients were described as having a slight brownish discoloration; in others the skin was muddy looking, or of a yellowish color. In three patients there was marked jaundice due to coincident hepatic disease. In two there was a peculiar profuse growth of hair; both of these cases were in young female children, the one reported by Cayley[6] was a girl of three years, in whom the eyebrows were thick and bushy, and there was a line of dark hair on the upper lip. Fox's[45] case was a girl, also of about three years, spoken of as gross and bloated, with the whole body surface remarkably hairy, especially about the genitals and pubic regions.

Sleeplessness is noted by Hausmann[16] as occurring in a case reported by him, and he quotes Addison who has spoken of its occurrence in Addison's disease. I have not noted this symptom in any of the other cases; on the contrary, the tendency of the disease is to give rise to dulness and apathy.

The temperature is usually normal, there being but three cases in which any marked rise of temperature above the normal was noted, and in these three the rises of temperature were due to coincident lung disease. Berdach[37] is inclined to think malignant disease of the suprarenal is often accompanied by a lowering of the temperature, and he has reported a case illustrating this view, and to prove his theory has experimented with dogs by removing both suprarenals, with the result of lowering the temperature in every case. The reported cases, however, do not bear out his view, and I have found only one other in which any record of the lowered bodily temperature was made. The temperature in all three cases in my list was either normal or slightly above the normal occasionally.

Hæmaturia has been noted twice in the 67 cases, and this is important, as it makes the differential diagnosis between renal and suprarenal tumors more difficult. In one case reported by Troisier,[32] the hæmorrhage was due to a secondary cauliflower growth in the renal pelvis, and the hæmorrhage in the second case was due, evidently, to cystic changes in the kidney, as there had been a tumor present in the renal region for eight years, during which time the hæmorrhage had lasted, and at the autopsy, besides a primary sarcoma of the suprarenal gland, the palpable tumor previously felt was found to be a cystic kidney.

The presence of a tumor was noted a good many times, but in such a way that it was impossible in some of them to tell whether it was not first seen post mortem, and as a careful description of its appearance, position and relations was never given, it would be useless to merely cite the number of times in which a tumor had been noticed.

I wish next to call attention to a certain number of cases in which the new-growth caused no symptoms referable to the suprarenal. Out of the 67 cases, 13 can be grouped under this heading. There were five in which the symptoms were entirely confined to the respiratory tract; one died of pneumonia, another of gangrene of the lung, two from extensive metastatic growths in the lung, the symptoms being entirely referred here, and in the fifth case, the only symptoms were an intense bronchitis and weakness.

Of the remaining eight cases several were interesting; for instance Wallman[33] reports a case of a young dragoon corporal who, admitted to the Hospital for the treatment of an ulcer over the shoulder blade, was suddenly attacked by œdema of the glottis. At the autopsy scirrhous changes in the right suprarenal gland were found. Greenhow[14] had a patient, a young girl aged twelve, who, two months previous to her death had scarlet fever, and following this a general œdema, but no symptom referable to the suprarenal, though she had quite an extensive growth in this gland. Wigglesworth[34] also reports the case of an old woman dying of "general decay following cerebral atrophy," and at the autopsy marked carcinomatous changes were found in the suprarenal gland. The remainder of the eight cases gave about the same history.

Diagnosis.

That the diagnosis is very difficult, and in some cases impossible, cannot be doubted, but I think with careful study of the cases which we may see, there are at least a certain number in which a diagnosis might be made. In considering the symptomatology, the most striking symptoms are the marked and steadily increasing loss of strength often accompanied by great languor and debility; the pain usually deeply seated in the abdominal cavity or radiating from one or the other renal regions; the marked emaciation and the various digestive and intestinal disturbances, added to which are in some cases the slight skin changes. If, in addition to these symptoms, there is a tumor present in one or the other renal regions we have a set of symptoms which, while not characteristic, are suggestive, and which would point to the possibility of a suprarenal origin. These symptoms are, unfortunately, not always present, and in the reported cases it is rare to find the whole set clearly marked, especially in combination with an abdominal tumor. The cases in which no abdominal tumor can be palpated are of course much more difficult to diagnose, and I doubt if in these a positive diagnosis can be made. Affleck and Leith[36] report a case of this kind, the patient having great and increasing weakness, gradual emaciation, loss of appetite, nausea and vomiting, and pain in the loins, passing thence around the abdomen and down into the thighs. There were no skin changes and no tumor palpable. This case was not diagnosed during life, though most of what we may call the cardinal symptoms were present.

The foregoing being the principal symptoms on which a diagnosis may be based, what are the other conditions which may simulate a suprarenal neoplasm?

The first of course to be studied are other changes occurring in the suprarenal gland itself. Of these the only ones which can be mistaken for a malignant tumor are blood cysts and occasionally tuberculosis, the so-called adenomata being usually very small and giving rise to no symptoms.

Blood cysts of the suprarenal are rare. Drouboix[59] has collected a number, and I have been able to find several others. Their origin is not at all clear, but they are probably the result of a necrosis in the centre of a new-growth, usually an adenoma with a subsequent hæmorrhage into the necrotic area. The symptoms in some of the reported cases are exactly those of a malignant tumor, and I do not see here how a differential diagnosis would be possible. I will quote two of the most striking ones as of interest. Carrington's[65] case occurred in a Swede aged 54 years. He gave a history of gradually increasing languor and weakness, and gradually increasing epigastric pain, for two months preceding his entrance into the Hospital. On admission he was weak and languid, somewhat emaciated, his mind wandering at times. No nausea or vomiting was complained of. On examination a tumor was felt in the epigastric region, descending with respiration and tender on pressure. There was a darkening of the skin around the nipples and on the penis and scrotum, and this pigmentation became more marked before his death, which occurred three weeks later. At the autopsy both adrenals were found changed into cysts, globular in form and about the size of an orange. On section they were found filled with a light brown, grumous altered blood. The cyst walls on microscopial examination were found composed of normal suprarenal tissue. Floersheim and Ouvry[60] also report a blood cyst of the left suprarenal which simulated a new-growth. The patient was a woman aged 36, who began to suffer three years before with pain in the lower portion of the left chest, becoming worse after eating and causing attacks of dyspnoea and a feeling of constriction. Examination revealed a hard mass in the left hypochondriac region in the position of the left kidney. The urine was normal. She was operated upon, a median incision being made, and the tumor was found to be a retroperitoneal cyst. It was punctured and three litres of a brownish fluid were evacuated. The walls of the cyst were then attached to the walls of the incision and the wound was dressed. The patient died of peritonitis, and at the autopsy the cyst was found to be retroperitoneal, the kidney lying below and attached to it by the convex border. The walls of the cyst which were from 6 to 7 mm. in thickness, were found on microscopical examination to be composed of suprarenal tissue.

That tuberculosis of the suprarenal might simulate a new-growth is also easy to conceive, though it is rare to find a palpable tumor in these cases. A. F. Jonas[61] has just published a case which demonstrates this. The patient had a palpable tumor in the renal region with symptoms pointing to a suprarenal tumor. Dr. Jonas did an exploratory operation and was able to remove the suprarenal growth which proved on examination to be tubercular. The patient got well.

Tumors of the kidney are most often confused with suprarenal growths, and among the collected cases I found eight in which the diagnosis of renal neoplasm had been

made. This is not surprising when we consider that the suprarenal tumor is retroperitoneal, and occupies the same position as would an enlarged kidney. The differential diagnosis is based on the difference in the symptoms complained of in the two conditions, and on the presence of hæmaturia accompanying the renal neoplasm. This symptom, according to most observers, occurs in about 50 per cent. of renal neoplasms, and its presence might be considered conclusive, though as we have seen above, hæmaturia was present with two cases of suprarenal tumor, in one due to a secondary carcinoma in the renal pelvis, and in the other to advanced cystic disease of the kidney.

Rarely the kidney may be felt displaced by the suprarenal tumor, as occurred in Case I of our series, though even when felt it is difficult to recognize as the kidney. This possibility as an aid to diagnosis has also been noted by Pawlik in an article on renal surgery in one of the German journals.

Tumors of the liver have also been diagnosed where the trouble was really in the suprarenal, though in these cases the diagnosis has been entirely based on the presence of a large tumor in the hepatic region, and careful consideration of the symptoms and a painstaking physical examination would, in most cases at least, serve to distinguish the two.

Other conditions might also simulate a suprarenal tumor, as Berdach[36] in his article discusses the possibility of differentiating from retroperitoneal glands or a pancreatic cyst or neoplasm. Especially with a pancreatic cyst one could imagine the diagnosis to be difficult, as here also we get the emaciation, epigastric distress and nausea and vomiting, but the tumor is usually differently situated, and there are other symptoms which do not occur with the suprarenal disease.

Having considered the diagnosis it may be of interest to review our cases again briefly.

In Case I it seems now that the diagnosis should have been made, as she had many symptoms pointing to the suprarenal origin of the tumor. The presence of the kidney-shaped prominence on the surface of the tumor, the complete absence of blood from the urine throughout the whole illness, the slight brownish discoloration of the skin and the steady loss of flesh and strength were all of importance.

Case II would have been more difficult to diagnose correctly, as the symptoms were not so definite, and save for the complaint of feeling weak and badly and the rapid loss of flesh, there were no definite symptoms pointing to the suprarenal origin.

Case III was also diagnosed by the surgical staff without hesitation as a renal new-growth, and it was not until the incision was made that its true character was seen.

TREATMENT.

The treatment must necessarily be surgical, and unfortunately there have not been enough cases operated upon to be able to draw any very definite conclusions from them, so the indications and probable prognosis will have to be largely obtained from a study of the symptoms, duration, and post-mortem discoveries.

One learns first from a study of the symptoms that the disease is insidious in its onset, which tends to make an early discovery of it rare, and when once developed the condition of the patient rapidly grows worse; and on this account any severe operation is more dangerous than it otherwise would be. That the course is a rapid one is shown in the fact that the average duration in 26 cases of carcinoma was, from the onset of the first symptom, 10.6 months, the least duration being 6 weeks and the longest 36 months. In sarcoma the average duration from the onset of the first symptom was even shorter, being but 6.7 months, the least duration one month and the greatest 13 months.

In examining the autopsy reports one finds there also several striking points which would evidently have an important bearing on the question of successful operation.

The first question which arises naturally when there are two organs of the same character in the body and one is to be removed, is what is the condition of the opposite organ? and when the retention of one is necessary to life this is a very vital question. This of course can only be answered in an incomplete way from the findings at autopsy, as necessarily in these cases the most ample time possible is given for the formation of metastases, but even with this the observer cannot but be struck with the great frequency with which both glands are involved, and also by the fact that in so many cases the glands on both sides are so nearly equal in size and general appearance, denoting either a simultaneous primary involvement or very early metastases. This is more especially marked in the carcinomata, there being in 30 cases where the side affected was noted 17 in which both glands were involved, the right side being alone affected in 6 and the left side in 7. Among the sarcomata this was not so marked; in 28 cases where the side was noted only 8 had both glands involved, the right alone being sarcomatous in 10 and the left in 10.

The frequency of metastases is also important, and the study of these from the post-mortem room is open to the same criticism, namely, that they had the longest possible time to develop, and that we should not be so likely to find them at an early operation. I attempted to get further light on this by studying the number of organs involved in the metastases and their apparent age, but found it impossible to get any reliable figures because of the incompleteness of the reports, but gathered enough to convince myself that the metastases in a good proportion of the cases occurred quite early, and were pretty widely diffused. In the carcinomata there were 28 cases where metastases were found in one or more organs, and in only three were they noted as not being present. The other six cases were so incompletely reported that their presence or absence could not be determined. In the sarcomata the metastases were not so frequent, being present in 14 cases, noted as not present in 6 cases and in 10 cases it was impossible to tell from the report whether present or not.

Among the carcinomata the organs most frequently affected were the lung in 15 cases, the kidney in 13 cases, the liver in 11 cases, the retroperitoneal glands in 7 cases, the stomach in 5 cases, the pleura and heart in 4 cases each, and almost every other organ in the body was noted as involved once or twice.

The sarcomata affected the liver in 6 cases, the kidney in 5

cases, the lung and the pleura each in 3 cases, and most of the other organs once or twice.

From these facts we may justly conclude, first, that an early operation is of vital importance, as, because of the insidious onset and rapid course, we will have to combat later, besides the difficulties of the operation itself, the lowered vitality and the lowered resistance of the patient. Second, that because of the probable early occurrence of metastases and the frequent involvement of both glands, the prognosis for final cure, even in the result of a successful operation, is unfavorable to say the least. Third, that because of the less frequent involvement of both glands, and the less frequent metastases, the prognosis in sarcomata is more favorable than in carcinomata.

The study of the difficulties occurring during the operation, and the results following it, naturally come next, and though we have but five from which to draw any conclusions, there are several interesting facts to be obtained from them. The cases are the three which I have reported, a case reported by Roberts,[56] of Philadelphia, with a fatal result, and two so-called suprarenal tumors removed by Knowsley Thornton,[63] with good results and briefly mentioned in his monograph "Surgery of the Kidneys." Only one of these can be used, as the other was undoubtedly a new-growth in an aberrant suprarenal gland in the kidney, for he speaks of the tumor as being surrounded by kidney tissue. Of these five, three resulted fatally: two immediately following the operation, and one in three weeks.

In Case I of our series the growth was firm and well outlined, and not adherent, and though some trouble was experienced in raising it from its bed and tying the vessels, the operation was not especially difficult, and except for the removal of the kidney with the tumor, gave no cause for anxiety, and as the result showed was perfectly successful. No troublesome hæmorrhage occurred during the removal. This case illustrates the most favorable growth that could be encountered. In our second case, however, a growth of a different character was found, illustrating well one of the difficulties which will be met, namely, a soft, friable tumor which when handled the least roughly breaks down and gives rise to almost uncontrollable hæmorrhage, besides making it impossible to remove it entirely. Dr. Roberts encountered the same difficulty in his case, and was compelled to abandon the operation because of the hæmorrhage before all of the growth had been removed, and his patient died three weeks later.

In Case III, while the tumor was removed entire, there was free hæmorrhage, and though the patient recovered from the anæsthesia, he died eight or nine hours later from shock, probably due to the long operation and his weakened condition.

In Dr. Thornton's case no account of the operation was given.

We find from these that the principal difficulties during the operation are free hæmorrhage and a tendency of the growth to break down during removal, and to these may be added the probability of dense adhesions, as in the pathological reports of many of the cases the tumor was noted as densely adherent to the surrounding organs, most often on the right side to the liver.

In spite, however, of the unfavorable outlook for a successful operation, it is best that at least an immediate exploratory operation should be advised in all cases where there is suspicion of a suprarenal new-growth being present, and this is even more true when a tumor is palpated, as we must remember that without operation the result will necessarily be rapidly fatal.

The question as to whether a further operation should be done in the event of finding a suprarenal tumor will depend on the character of the growth itself, the condition of the other gland, the absence of any visible metastases and the absence of dense adhesions. If the further operation is decided upon it is wise to remove the corresponding kidney, as we have seen that in 31 cases of carcinoma metastases were present 11 times.

The final result in our one successful case has been good so far, the patient being healthy and with no signs of any return of the growth.

Summary.

To summarize we find the following facts true: 1, that while malignant tumors of the suprarenal gland are rare, they should be considered as one of the factors to be eliminated in the presence of an abdominal tumor; 2, that they are somewhat more common in the male sex; 3, that while in a certain proportion the symptoms are fairly well marked, there are many in which no symptom points to the suprarenal origin; 4, that rapid loss of strength, debility, emaciation, digestive disturbances and abdominal pain are the most prominent symptoms; 5, that skin changes are rather the exception than the rule; 6, that they run a rapid course, the duration being shorter than usual with a neoplasm in other organs; 7, that the diagnosis is impossible in many, and difficult in all, cases; 8, that a differential diagnosis must be made from other suprarenal diseases, from renal tumors, from hepatic tumors, from diseased retroperitoneal glands, and from cysts and new growths of the pancreas; 9, that the prognosis is always serious, even following a successful operation, from the great frequency with which both glands are found involved, and the tendency to early metastases; 10, that operation gives the only hope of relief, and that it has been successful in two cases; 11, that the principal difficulties in the operation are, the friability of the tumor, the great tendency to hæmorrhage, and the frequency of adhesions.

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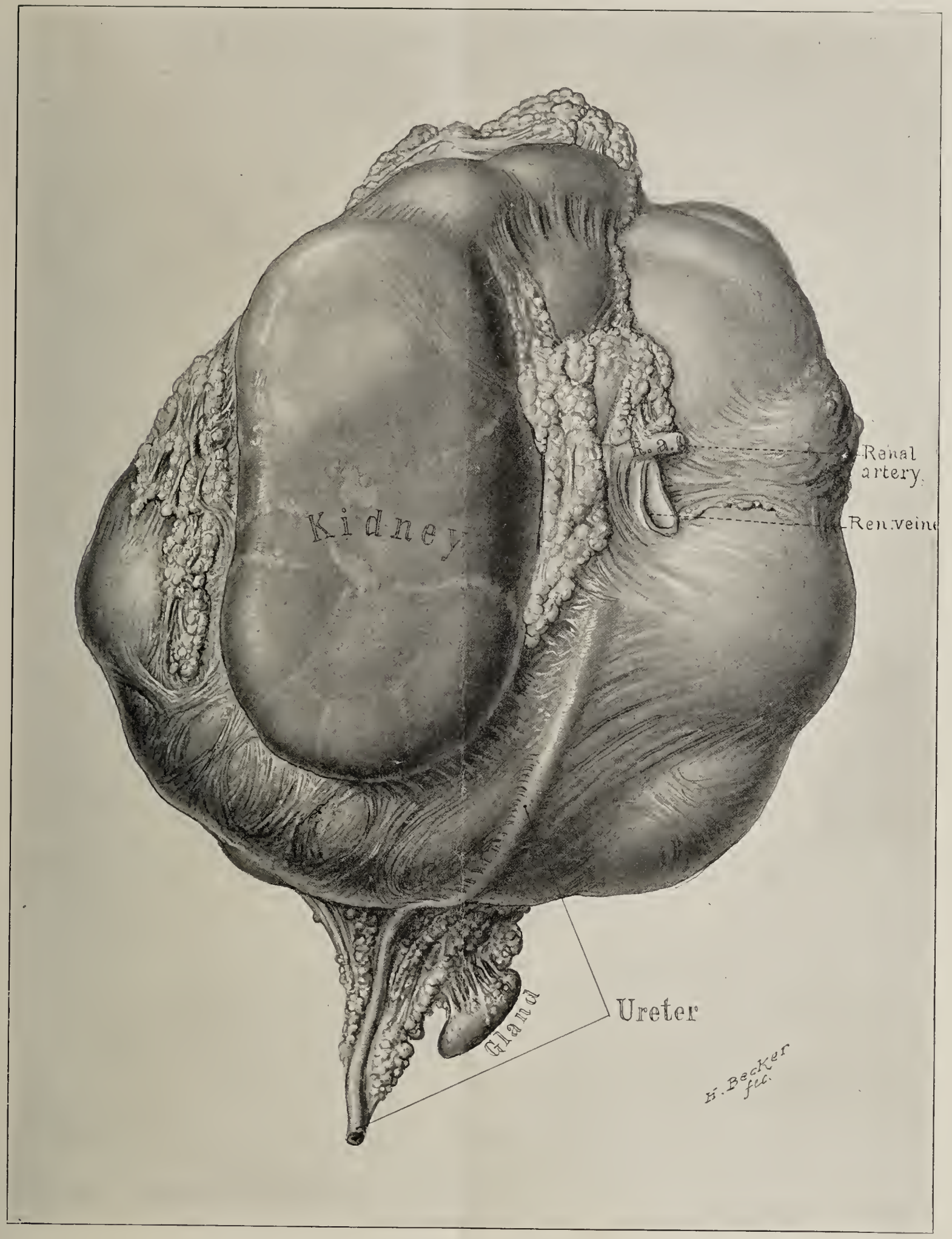


FIG. 1.—Tumor with kidney attached. Natural size. Case No. 1.



Fig. 2.—Same tumor cut in two. Shows the gelatinous contents of cystic cavity. The smaller size is due to the hardening process, as is also the dark color of the gelatinous material contained in the cyst.

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THE BACTERIOLOGY OF THE CAVITY OF THE CORPUS UTERI OF THE NON-PREGNANT WOMAN. A REPORT OF 68 CASES.

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So much has recently been written concerning the bacteria of the female genital tract that unless one proposes to publish a book upon the subject, as has been done by Menge and Krönig, a complete and careful review of all the literature relating to it is impracticable. I will refer those who wish to have this, to the work of the above-named authors, "Bakteriologie des weiblichen Genitaltractus, Leipzig, 1897." I will here briefly review the work done by the more prominent investigators upon the bacteriology of the uterine cavity, and then add the data obtained by my own investigations. This work relates only to bacteriological examinations of the cavity of the corpus uteri, but in order to make some of my conclusions clear I will briefly give the status of the bacteriology of the vagina and cervix at the present time.

The vaginæ of both pregnant and non-pregnant women can be regarded as being, under normal circumstances, free from pathogenic bacteria. The introitus vaginæ is the outer boundary of this aseptic zone. The normal vagina contains its peculiar micro-organisms, but the pathogenic bacteria, when introduced into it, quickly disappear. The abnormal cases in which the vagina may contain pathogenic bacteria are cases of gonorrhœa, acute wound infections extending into the vagina, where the secretions of infected uteri, etc., are being constantly poured into the vagina, those cases in which the vagina contains dead nutrient media as in carcinoma of the cervix uteri with hæmorrhage and necrosis, cases of retained placenta, of necrotic submucous myomata, uterine polypi, and in tuberculosis of the vagina. This, in general, is in accordance with the views of Döderlein, Menge, Krönig, Williams and others, and the weight of evidence is decidedly in its favor. Opposed to this view are Ahlfeld, Kaltenbach, Walthard, Vahle, Kollman and others, who think that the streptococcus and the staphylococcus pyogenes, the colon bacillus and other pathogenic bacteria are to be found in a large percentage of all vaginæ.

The cervical canal is likewise, under usual circumstances, free from pathogenic bacteria, and from a point at or just above the external os contains no bacteria whatever. The gonococcus of Neisser and possibly the bacillus of tuberculosis alone have the faculty of invading unaided the normal

cervical canal, but under conditions mentioned in connection with the vagina, that is, a necrotic or patulous cervix coupled with dead nutrient material in its canal along with similar disturbances of the aseptic properties of the vagina, other bacteria, indeed the streptococcus and staphylococcus pyogenes, may invade the cervix without their introduction by means of external agencies.

The mucosa of the corpus uteri may either be free from or show inflammatory changes, and it is well in studying the bacteria of the cavity of the uterus to classify the cases according to whether the mucosa shows this endometritis or not. Most writers classify endometritis into *glandular* where the uterine glands show hypertrophic or hyperplastic changes without infiltration of the mucosa with small round cells or polymorphonuclear leucocytes, and into *interstitial* where this infiltration occurs. As most investigators agree that bacteria are not present in the glandular type of endometritis, and as in many cases this form of endometritis seems to be not dependent upon bacteria, I think it well to follow the classification made by Dr. T. S. Cullen, and will speak only of endometritis in the cases where this infiltration occurs. I will follow his subdivision further in classifying it into acute and chronic with the intermediate subacute stage. In acute endometritis there are changes in the epithelium, infiltration of the mucosa with small round cells and polymorphonuclear leucocytes and increase in the number of blood-vessels without increase in the connective-tissue elements. In chronic endometritis there is less change in the epithelium, an infiltration of the mucosa with small round cells, increase in connective tissue, thickening of the walls of the blood-vessels, and generally atrophic changes in the uterine glands. When the uterine cavity contains a considerable quantity of pent-up pus so that its wall may be likened to the sac of an abscess cavity the condition is known as pyometra. Physometra or tympania uteri is the condition in which the uterine cavity contains gas.

In the autumn of 1894, at the suggestion of Prof. H. A. Kelly, and of Dr. Jno. G. Clark, then resident gynæcologist of the Johns Hopkins Hospital, I began the bacteriological examination of the body cavity of uteri removed by the method then in vogue in this clinic and in America generally, *i. e.* supravaginal amputation of the uterus. Circumstances prevented the examination of many of the cases operated upon, and absence from the Hospital and other causes prevented me from securing the number desired. However, I have examined the body cavity of sixty-eight uteri removed for a variety of causes, and I give in the table a summary of the results obtained. The relative numbers of cases of carcinoma, myoma, etc., examined do not represent the proportion of such cases operated upon in the Hospital. Very few of the carcinoma cases were examined bacteriologically, as the bacteriological examination destroyed, to a certain extent, the histological value of the specimen. The technique observed in making the bacteriological examination was as follows: As soon after the removal of the specimen as possible, and before it was handled, to burn thoroughly the amputated end of the organ, and then invade the cavity through the cervical canal with a platinum loop which had been heated to redness. As a rule, cover-glass preparations of the secretions thus obtained were stained and examined microscopically, and cultures made upon various nutrient media. The cover-glasses were stained for bacteria by the usual methods. Gram's method of staining and the usual stain for the bacillus tuberculosis were used where indicated. The cultures were made upon agar slants or Petri dishes, stab cultures upon glucose agar and acid gelatin, and smears upon cyst-fluid agar or ascitic fluid agar or urine blood-serum agar, when these media could be obtained. I have also prepared a table containing a brief abstract of the histories of the cases, trying in these abstracts to embody everything relating to the nature of infection the operation, the convalescence, and the histological and bacteriological reports. As this table was too voluminous to be included in this article, the table given was prepared from it. This was deemed advisable, as Sänger and other prominent writers have emphasized the fact that clinical signs are as much or more to be depended upon in diagnosing gonorrhœa in women than the microscopical examination of the secretions, and undoubtedly a combination of clinical signs and the bacteriological examination is the true method in making a diagnosis.

In glancing over the table, we see that of the 68 cases, 53 showed changes of an inflammatory nature as indicated either by endometritis, or by inflammatory changes in the uterine adnexa. The uterine mucosæ in 51 of the cases were examined histologically, and 19 of these showed an acute, or subacute, and 12 a chronic endometritis. Eighteen of the cases showed no inflammatory changes in the endometrium. In *none* of the cases where there was no endometritis were bacteria found in either the stained specimens or in cultures. This, as we shall see later, corresponds entirely with the prevailing views upon the subject, *i. e.* that the body cavity of the normal uterus is free from bacteria. Concerning the bacteria found: the gonococcus was found seven times, the streptococcus pyogenes once, the staphylococcus pyogenes aureus once, the staphylococcus pyogenes albus twice, the bacillus of tuberculosis twice, and unidentified saprophytic bacteria four times. We have just stated that the gonococcus was found seven times, three times by cultures and cover-glass preparations, and four times in the stained specimens only. The micro-organism was found five times in the cavity of the corpus uteri, and twice in the pus from a pyosalpinx or ovarian abscess, and not in the uterine cavity. In all of these cases the typical biscuit-shaped diplococci were found in the pus in large numbers, lying both intra- and extra-cellularly, and decolorized by Gram's stain. The cultures were also characteristic. In another case the micro-organisms were probably found, but in such small numbers that Gram's stain was unsatisfactory. It was never found in the chronic cases of endometritis. In one case, where the gonococcus alone was found, there was an abscess in the uterine muscle, although the abscess cavity was not proven to contain the micro-organism. This cavity was not discovered until sections were cut for histological examination. One case showed a gonorrhœal pyometra. The woman gave a history of an infection following a miscarriage. Upon dilating the cervical canal, about three drams of a thin, odorless, yellowish pus escaped.

This pus contained gonococci in large numbers. There was in this case a stenosis of the os uteri, probably either by a dilated cervical gland, or swelling of the mucosa as a result of the inflammation. Another woman, who gave a history of an infection immediately following a miscarriage, proved to be infected by the gonococcus alone. The micro-organisms were found at the operation in the secretions from Bartholin's glands, urethra, vagina, external os uteri, the cavity of the uterus, the acutely inflamed tubes, and in pus found in the peritoneal cavity among coils of intestines. The gonococcus was never found accompanied by other bacteria. It was found once in a myomatous uterus.

Of all the bacteria, the gonococcus is by far the most frequent invader of the uterine cavity. This micro-organism has the faculty of invading the uterus through the previously healthy cervical canal, causing an acute endometritis, and subsequently by direct extension along the mucous membrane of the genital tract inflammatory conditions of the Fallopian tubes, ovaries, and peritoneum. It probably always gains entrance to the uterine cavity through the cervix. In the uterus it generally limits its ravages to the endometrium, although it apparently penetrates in a small number of cases into the muscular structure of the uterus, causing a metritis and abscess formation. This is in accordance with the views of Wertheim, who found the microbe in the stroma of the uterine mucosa, and of Madlener, who found it in the uterine muscle. The case of mine would point to the same abscess formation in the uterine muscle. The acute purulent endometritis which it causes after a time becomes chronic or heals. From the uterine cavity it frequently extends along the mucosa, and is the cause of most cases of pyosalpinx, pelvic adhesions, pelvic encysted peritonitis, of circumscribed pelvic abscess, ovarian abscess, and probably of many cases of hydrosalpinx. It can, from the uterine cavity, get into the blood-current and thus cause a systemic gonorrhœal infection. It apparently lives but a short time in the abscesses which it causes, but can, probably, exist much longer in the mucous membrane of the uterus. It is noteworthy that in most cases of chronic gonorrhœal endometritis the micro-organism cannot be found by bacteriological examination. Sänger emphasized this fact and recently Broese and Schiller came to the same conclusion from the examination of 271 cases. Every one who has attempted to cultivate the gonococcus has noted the great difference in various cases with which the micro-organism grows. The fact that one cannot cultivate it, and does not find it in stained specimens, is not proof that it does not exist in a given case. Where the micro-organism occurs in very small numbers, Gram's stain, by which it is identified, is very unsatisfactory. Clinical signs point to its existence for long periods of time, and it may be given renewed vitality from time to time by a change in its nutrient media, as in the puerperium, operations on the uterine mucosa, etc. It appears to be more apt to invade the puerperal or menstruating uterus, and is more apt to be than is usually thought the cause of miscarriages. Interesting in this connection are the two cases previously mentioned, in both of which the women gave histories of an infection immediately following a miscarriage, and both of which proved to be infections by the gonococcus alone. Neumann has recently reported a case where he examined a woman who had a gonorrhœal infection, and in whose decidua he found the gonococcus. Maslowsky also has recently reported a most interesting case, where a premature labor was caused by an "Endometritis decidualis interstitialis gonorrhoica." He found the gonococci in the decidua vera, which was infiltrated with small round cells. Fehling, Winckel, Krönig, and other authors believe this micro-organism to be a fruitful cause of miscarriage. It probably does not, by its presence, favor the entrance of other bacteria into the uterus, indeed, Menge and Wertheim believe that it will not tolerate other bacteria in the same field with it. In my seven cases it was not accompanied by other bacteria, nor in the cases which gave a gonorrhœal history were other micro-organisms found. It may be the cause of a pyometra. It is comparatively harmless to the peritoneum, for, although where it is being constantly poured into the peritoneal cavity, it always gives rise to a localized and perhaps, occasionally, to a general peritonitis, I do not find a well-authenticated case of death due to a gonorrhœal peritonitis. In one of the cases reported here, and in several occurring at various times in the clinic, where gonorrhœal pus was found free in the peritoneal cavity, after the removal of the pus and its source, the women recovered without any greater rise of temperature than one would expect in a clean case. In many of the cases of myomata, with inflammatory conditions of the appendages, this micro-organism is, probably, responsible for the inflammation. One of our cases, in which the gonococcus was found, was a case of myoma uteri.

The streptococcus pyogenes was found but once. This case was a negro woman with a large sloughing submucous uterine myoma. She entered the Hospital in an extremely weak condition—pulse 136, temperature 102°–104° F.—and died during the operation for removal of the myomatous uterus. The streptococcus, along with an unidentified bacillus, was found in the uterine cavity. There was undoubtedly a systemic infection by the streptococcus, although as no autopsy could be obtained this could not be proven. In this case the infection evidently occurred through the vagina, due to the following conditions: An open cervical canal due to the encroachment of the myoma, and to the uterus, cervix and vagina being filled with decomposing blood and necrotic myomatous material. Thus by overcoming the protective functions of the cervical canal and vagina, and by furnishing the bacteria with suitable nutrient media, this micro-organism which cannot under ordinary circumstances invade the uterus, found its way in and with a fatal result. This case corresponds entirely with the views of Menge and Krönig and with a case reported by Dr. Maurice H. Richardson in the *Boston Medical and Surgical Journal*, September, 1893, where a woman who had a facial erysipelas, and who was bleeding from a submucous myoma, died of a streptococcic peritonitis due to the invasion of the bacteria most probably through the genital tract. The streptococcus is of especial importance in puerperal infections but can, as we have seen above, cause infection in other conditions of the uterus, as in cases of myomata, carcinomata, necrotic polypi, and of course in operations upon the uterus, criminal abortions, etc. It is,

perhaps, in puerperal conditions nearly always introduced into the uterus by external agents, but can, as proven by Krönig's statistics, find its way into the puerperal uterus by growing in where no vaginal examinations have been made. In these cases it probably exists on the skin, clothing, etc., and finds in the vagina and cervix the suitable conditions for its extension. From the uterus it can gain entrance into the general organism through the lymphatics and the blood-vessels. In cases which do not run a rapidly fatal course, dense pelvic exudates in the connective tissue of the pelvis, filling the whole or part of the pelvis, and containing frequently small abscesses, are characteristic of a streptococcic uterine infection. This micro-organism may enter the peritoneal cavity along the lumen of the Fallopian tubes, although the more common route of invasion seems to be by way of the lymphatics, thrombosed vessels and abscess formation in the uterine walls. It produces frequently a systemic infection. Pyosalpinx is not usually the result of a streptococcus infection. In the normal non-puerperal uterus the streptococcus probably cannot gain entrance into its cavity without the aid of external agents.

The bacillus of tuberculosis was found by histological examination to be the cause of the endometritis in two of the 31 cases, nearly 6.5 per cent. In these two cases no tuberculous processes were found in the Fallopian tubes, and in another case the hysterectomy was performed for tuberculosis of the tubes, when the endometrium of the uterus was free from disease. These two cases would seem to show that primary tuberculosis of the endometrium may occur, the bacteria gaining entrance through the vagina and cervix. Most writers believe this to be the case. Most cases of tuberculosis of the endometrium are, however, secondary to processes in the tubes, and this as secondary to tuberculosis in other parts of the body. Tuberculosis of the endometrium seems to stop suddenly at the internal os, and pyometra frequently results as a product of tubercular endometritis.

The staphylococcus pyogenes aureus was found once, and the staphylococcus pyogenes albus twice, in the uterine cavity. The former was found in a pyometra along with an unidentified bacillus in a case of carcinoma of the cervix. The woman gave no evidence of a general infection by this micro-organism. The staphylococcus albus was found once following the removal of a submucous myoma where, after five or six days, the woman's temperature rising to 104° quite suddenly, a bacteriological examination was made by means of Döderlein's tube, and the staphylococcus was found both in cultures and on slides, together with an unidentified bacillus. In the second case the micro-organism was evidently carried in by instruments. Here the woman was curetted before removing the uterus. The micro-organism was found by means of cultures in small numbers in the uterine cavity, while the pus from the pyosalpinx was sterile. The staphylococcus pyogenes like the streptococcus can invade the cavity of the uterus probably only when the protective properties of the vagina and cervix are overcome, as in cases of carcinomata, myomata, etc., or when carried in by operative procedures. Once in the cavity of the uterus, if the endometrium is unwounded and under normal conditions, it soon disappears; but if the mucosa is wounded, or there is dead nutrient material there, it causes suppurative processes. It probably causes miscarriages by producing a deciduitis, as in a case reported by Neumann, or it may cause a general systemic infection, as in Strünckman's case. It is more rarely found in the uterine cavity than the gonococcus and streptococcus, and probably than the bacillus of tuberculosis.

The other bacteria found were unidentified and were, probably, saprophytes. One was found in the streptococcus case, two in cases of pyometra, once in combination with the staphylococcus pyogenes aureus, and one in the case of submucous myoma along with the staphylococcus pyogenes albus.

In looking at our cases from a clinical standpoint we find a result that may not be uninteresting. Making a diagnosis as to the mode of infection from the history of the case, coupled with the bacteriological examination, we find that of the 53 cases showing inflammatory changes, 26 were, probably, of gonorrhœal origin, 12 of puerperal origin, 3 due to tuberculosis, 4 to myomata or carcinomata, 4 to previous operations, and 2 unclassified. Some of the cases giving a history of puerperal infection undoubtedly owed their origin to the gonococcus. In our cases, therefore, the gonococcus was the probable cause of infection in more than one-half of them.

A few interesting points may be gained from the table. In two cases there was a hydrosalpinx and pyosalpinx combined in the same patient. Most writers think that pyosalpinx is due to bacteria, and many contend that bacteria have nothing to do with hydrosalpinx, and that hydrosalpinx is never the result of a purulent salpingitis. Our two cases would point to one and the same cause for both conditions. We see further that in four cases of hydrosalpinx, three of pyosalpinx, and two of ovarian abscess, there was, on histological examination, a normal uterine mucosa, *i. e.* no infiltration with small round cells, or polymorphonuclear leucocytes. There are only two explanations for this: one, that the infection did not occur *via* the uterine cavity, and the other that the preëxisting endometritis had healed. The latter is, in most cases, the most plausible explanation. We see cases of healed salpingitis also, hence it is more than probable that hydrosalpinx is frequently the end product of a suppurative salpingitis. Three deaths occurred, and it is instructive to investigate the causes: one, the streptococcus case was in a desperate condition when operated upon, and died on the table. The second died as the result of an intestinal perforation and the following peritonitis. The sigmoid flexure of the colon was injured during the operation and was sutured. This suturing gave way, and with a fatal result. The third was the result of an infection with the staphylococcus pyogenes albus, and streptococcus pyogenes secondary to drainage in a case, probably, originally gonorrhœal. The cultures and stained preparations at the time of operation showed no bacteria. Drainage was through the vagina, and also through the abdominal wound. The staphylococcus infection occurred through the vagina, as proven by bacteriological examination before death. Both micro-organisms were found in the peritoneal cavity at autopsy. Death then in one of the two fatal cases possible to have been avoided was due to drainage. In the other case drainage

would possibly have saved the life of the patient, but was not indicated at the time, as the bowel was supposedly well sutured.

Let us see how our results correspond with the results obtained by the various investigators. Winter was among the first to examine bacteriologically the cavity of the uterus. As a result of his investigations he came to the conclusion that "the healthy body cavity of the uterus contains no bacteria." His work was done upon uteri which had been removed for myomata, or upon those removed by panhysterectomy. He did not examine the mucosæ of these uteri histologically. Brandt, in cases of symptomatic endometritis, found in 30 per cent. of all his cases pyogenic bacteria, and in the 25 cases examined only 3 were free from bacteria. Péraire, who also worked with cases of endometritis, found practically the same thing. Pfannenstiel, in both interstitial and glandular chronic endometritis, found no bacteria. Bumm states that in the chronic glandular and interstitial endometritis of non-pregnant women bacteria are in most cases not present, but that in a small number of cases one finds bacteria, which he regards as only an *accidental* accompaniment of these conditions, and which can change according to the character of the secretion. Wertheim says that the gonorrhœal infection of the uterus causes always a purulent catarrh which, when it becomes chronic, can produce a hypertrophy and hyperplasia of the uterine glands, and that the inflammation may extend to the myometrium. Gottschalk and Immerswahr found in cases of endometritis that bacteria were present in 65 per cent. of the uteri, and found frequently the staphylococcus pyogenes. They thought that the presence of the gonococcus predisposes to the subsequent invasion of the staphylococcus. Madlener went further than Wertheim, who had found the gonococcus in the stroma of the uterine mucosa, and found this micro-organism in the uterine muscle. He says that the gonococcus of Neisser has the faculty of penetrating the musculature of the uterus from the endometrium, and thus cause inflammation. Bumm, however, states that he examined Madlener's preparations and was not convinced that gonococci were present. Boije found bacteria present in 19 of 30 cases, and came to the conclusion that bacteria are the causes of interstitial endometritis, but not of glandular. Menge examined the body cavity of 119 uteri which had been removed for a variety of causes. Thirty-nine of these cases showed round-cell infiltration of the uterine mucosa, and 11 of the 39 cases were in carcinoma of the cervix. As a result of his investigations he comes to the conclusion that neither in the secretions nor in the tissue of the mucosa of the cavity of the corpus uteri, in cases showing no endometritis or only the glandular form, do bacteria exist which we can cultivate. In his 119 cases he found bacteria only 11 times. One case was that of a submucous necrotic myoma; two were cases of gonorrhœa; two, of tuberculosis of the endometrium; one, an unknown bacillus in an acute case; and the remaining five were in cases of pyometra. Opitz examined 10 cases and found all free from bacteria. Kollman reports a case of a myomatous uterus, in which the mucosa showed no inflammatory changes where he found bacteria present in the cavity. These were not identified. Warbasse, in 17 cases of chronic endometritis, found bacteria present in 5 of them. He concluded, however, that the micro-organisms were not the cause of the endometritis, and that it is no more necessary to look for a bacterial origin of chronic endometritis than in inflammation of other glandular organs.

In looking over the literature of the subject we find that the following bacteria have been found in the uterine cavity in its various inflammatory conditions, *viz.* gonococcus of Neisser, streptococcus pyogenes, staphylococcus pyogenes aureus, albus and epidermidis albus, bacillus of tuberculosis, bacillus coli communis, bacillus ærogenes capsulatus, bacillus of tetanus, bacillus typhosus, diplococcus lanceolatus, and many saprophytic and unidentified bacteria. All of these bacteria have been found in the puerperal uterus. In the non-pregnant and non-puerperal uterus the only micro-organisms reported to have been found are the gonococcus, the streptococcus pyogenes, the staphylococcus pyogenes, the tubercle bacillus and saprophytic bacteria. The cavity of the corpus uteri of both the pregnant and non-pregnant woman under normal conditions is free from bactera. The boundary line between this bacteria-containing and bacteria-free zone is the external os uteri. The only bacteria which can invade the cavity of the uterus through the external os without the help of external agencies, and under normal conditions are the gonococcus of Neisser and the bacillus of tuberculosis. Nearly all of the best-known investigators are agreed upon this view. Upon the causes of inflammation of the mucosa of the uterus and the bacteria which may be found there in cases of endometritis there is not such a unanimity of opinion. It is of vital importance to the surgeon to know if the streptococcus pyogenes, the staphylococcus pyogenes or other pathogenic bacteria do exist in the uterine cavity, and if so, under what conditions he may expect to find them, and what may be done to guard against carrying these micro-organisms into the peritoneal cavity or exposed wound surfaces. In the class of cases previously mentioned, where the protective functions of the vagina and cervix are totally, or in a measure, lost by means of a prolapsus, or very much relaxed vaginal outlet, an open cervical canal, or destruction of the cervix by carcinoma, where the cervix and vagina are filled with dead nutrient material as necrotic placental remains, carcinomata, sloughing myomata or polypi, both the pathogenic and saprophytic bacteria are liable to be encountered. Following also, of course, recent operative procedures upon the vagina or uterus, an acute wound infection may exist and thus infect the peritoneum of the patient upon whom a laparotomy is subsequently done. In puerperal sepsis, of course, also this danger exists. The gonococcus will also be frequently encountered in inflammatory cases, but may be disregarded so far as operative procedures are concerned.

In uncomplicated cases of hystero-myomectomy, hysterectomy for inflammatory cases, or ovarian tumors, operations for extra-uterine pregnancies, and in all such cases where the vagina and cervix are normal, except, probably, for the invasion of the gonococcus, *the safest route so far as infection is concerned is the abdominal.*

In operations for carcinomata, especially where the cervix is necrosed, in submucous myomata, especially if the tumor

encroaches on the cervix, and in similar cases of polypi, etc., in puerperal cases upon whom a hysterectomy is performed, and in circumscribed pelvic abscesses which are liable to be secondarily infected from the intestine, *the safest route with regard to infection is the vaginal.*

As the external genitalia and the surrounding parts are even more liable to contain pathogenic bacteria than the abdominal wall, the cleansing and disinfection of these parts is as imperative as the cleansing of the abdomen preparatory to operation.

Drainage through the vaginal vault in cases of laparotomy unless imperative to arrest hæmorrhage, or in cases of wounded intestine where the suturing is unsatisfactory, is almost as much to be deprecated as drainage through the abdominal wall. The vaginal vault should be, when possible, left intact.

In conclusion, I wish to thank Drs. Kelly, Russell, Clark and Ramsay for their aid and encouragement in my work, and Drs. Cullen and Hurdon for the pathological reports of the cases.

Total number of cases examined bacteriologically	68
No. of cases of an inflammatory nature	53
No. of cases of uterine myomata	24
No. of cases of carcinoma of cervix uteri	3
No. of cases of probable puerperal infection as shown by the history	12
No. of cases of *probable* gonorrhœal infection as shown by the the history	19
No. of cases of *positive* gonorrhœal infection	7
No. of cases where endometrium examined histologically	51
No. of cases of endometritis with small round-cell infiltration only	12
No. of cases of endometritis with small round-cell and polymorphonuclear cell infiltration	19
No. of cases where there were was no endometritis	18
No. of cases of pyometra due to: gonococcus	1
staphylococcus and saprophytes	1
saprophytes only	2
No. of cases of abscess in uterine wall (muscle)	3
No. of cases of tubercular endometritis	2
No. of cases where the streptococcus was found	1
No. of cases where the staphylococcus was found: albus	2
aureus	1
No. of cases where unknown bacteria were found	4
No. of cases of myoma uteri accompanied by endometritis or inflamed adnexa	9
No. of cases of myoma uteri where the endometrium showed no inflammatory change	11
No. of cases of pyosalpinx	24
No. of cases of hydrosalpinx	9
No. of cases of pelvic adhesions only	9
No. of cases of circumscribed pelvic abscess	3
No. of cases of ovarian abscess	5
No. of cases of hæmatosalpinx	2
No. of cases of hydrosalpinx of one tube and pyosalpinx of the other	2
No. of cases of hydrosalpinx with no endometritis	4
No. of cases of pyosalpinx with no endometritis	3
No. of cases of ovarian abscess with no endometritis	2
No. of cases of infection through the cervical canal due to myomata	2
No. of cases of infection through the cervical canal due to carcinoma of cervix uteri	2
No. of cases of infection through the cervical canal due to operation	1
No. of cases in which inflammatory changes in the uterine adnexa were due to previous operation	3
No. of cases of *probable* gonorrhœal infection where endometritis was found	12
No. of cases of *probable* puerperal infection where endometritis was found	6
No. of deaths due to: drainage	1
intestinal perforation	1
streptococci infection	1

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THE PRESENCE OF FOREIGN BODIES IN THE VERMIFORM APPENDIX, WITH ESPECIAL REFERENCE TO POINTED BODIES.

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The suggestion of a pin being the cause of an appendicular abscess as brought out in the history of a patient in the Gynæcological Wards of the Johns Hopkins Hospital has led, with Dr. Kelly's encouragement, to this inquiry, as to foreign bodies in general as a cause of appendicitis, and especially pointed bodies.

The patient, a girl aged twenty, was admitted to the service of Dr. Kelly with a sinus in the abdominal wall at the right iliac fossa. It was stated that, when about six or seven years of age, she had pain in the right iliac region followed by an abscess developing sufficiently to be opened in forty-eight hours. The wound was dressed every day thereafter, and some time later a pin was found in the discharge from the wound and the whole trouble was attributed to that. There was no further trouble until about four years ago, since when she has had repeated attacks of appendicitis more or less typical.

As to the frequency with which foreign bodies other than fæcal masses are found in the vermiform appendix, our opinions have changed greatly in the last ten years; at one time the presence of a foreign body was thought essential to an appendicitis, and the classical orange, date, or cherry seed were often described. Undoubtedly many of them, so eagerly sought, were nothing more than fæcal concretions which are likely to assume these shapes, and unless carefully examined easily deceive the observer. From this extreme the other has now been reached. Many writers at the present day go so far as to state that foreign bodies are never found as the cause of appendicitis, and this attitude would seem to find some justification in the following facts.

Fitz,* in 1886, collected 152 cases of perforative appendicitis, and found 12 per cent. of foreign bodies with 47 per cent. of fæcal concretions while Hawkins,† in 1895, in 67 fatal cases did not find a single foreign body. In 250 cases of appendicitis in the Johns Hopkins Hospital in the past ten years, there has been only one foreign body—a segment of tapeworm.

With this object in view I have collected 1400 cases from various sources in the last ten years, and find about 7 per cent. of true foreign bodies; while in 700 of these cases, in which a definite statement was made as to the nature of the foreign body, there were 45 per cent. of fæcal concretions. The older statistics invariably give a higher percentage of foreign bodies.

While so many accounts are evidently untrustworthy because of lack of careful examination, the undoubted occurrence of many queer and interesting objects as shot, pins, worms, gallstones, a tooth, or a piece of bone, has been recorded; and even the discarded grape seed or cherry stone is occasionally seen. Fenger‡ had a case in which two grape seeds and an oat husk were found, and Welch once met with a date seed. Osler,§ in ten years' experience in Montreal, found foreign bodies only

* Fitz: Transactions of the Association of American Physicians, 1886, I, 110.

† Hawkins: On Diseases of the Vermiform Appendix, London, 1895.

‡ Fenger: American Journal of Obstetrics, 1893, XXVIII, 168.

§ Osler: Principles and Practice of Medicine, 1898, 520.

twice; in one instance five apple pips, and in another eight snipe shot. Stone,* of Omaha, and Ransohoff,* of Cincinnati, each removed an appendix containing a bullet (Fig. 6) as the exciting cause. A case is reported by Holmes,† in which 122 robin shot were present in the appendix of an old man dead of pneumothorax, who, during life, had had no symptoms referable to the appendix; but who, it is stated, was very fond of game. Interesting in connection with this is the following observation in the Mémoires de l'Académie Royale de Chirurgie‡ in 1743. "One notices sometimes in opening the bodies of persons who, during life, have eaten a great deal of game that there is collected in the intestines, and especially in the cæcal appendix, a great quantity of shot, without those persons having had the least inconvenience."

Gall-stones are not infrequent and cases are cited by Gibbons,§ Nelson‖ and Ulloa y Giralt.¶ Fæcal concretions may so closely resemble gall-stones that it is impossible to distinguish between them except by chemical analysis. For the sake of exactness too much stress cannot be laid on this. A specimen kindly loaned by Dr. Rogers, of Memphis (Fig. 4), well illustrates this. The patient, a man aged twenty-two, had an attack of hepatic colic, with intense pain over region of gall-bladder, jaundice, vomiting, fever, etc. His trouble subsided and then after a few days symptoms of appendicitis appeared, which likewise subsided, leaving slight tenderness in the right iliac fossa. On examination three small nodules could be felt at the site of the appendix. Operation revealed an appendix distended with three bodies looking exactly like gall-stones, and such Dr. Rogers very rightly supposed them to be. Chemical examination by Dr. Thomas R. Brown, however, showed that they contained no cholesterin and no bile pigments nor salts, but were made up mostly of organic matter with carbonates and phosphates of calcium and magnesium.

One class of foreign bodies, however, far more common and more important than any of these, may be grouped together as pointed bodies. The only explanation that can be offered for their presence is in their shape, which allows them to become engaged in the cæcal opening of the appendix more readily.

A not uncommon occupant of the appendix is a lumbricoid worm. Numerous cases are recorded. One of the earliest of these is that of Blackadder** in 1824. A man in apparent good health was seized with sudden abdominal pain, so intense that he fell to the ground and died in less than four hours. At autopsy nothing was found except that into the appendix which was remarkably increased in length and thickness and felt like a firm cord, a large lumbricus had forced its way until only an inch of its tail projected into the cæcum. There were no other lumbrici in the alimentary canal.

Dr. C. F. Brower,* of Virginia, possesses the specimen, of which a drawing is shown (Fig. 1). The patient, a child of twelve years, presented symptoms of a mild attack of appendicitis. Dr. Brower operated 30 hours after onset of symptoms, removing the appendix with a portion of adherent omentum. The worm, being still in the appendix, was divided by the scissors and half of it then withdrawn from the cæcum. The appendix was gangrenous for an inch and a half at its distal end, and at one point was on the verge of perforation. Recovery was uneventful.

The only foreign body observed in this Hospital in 250 cases was a segment of tapeworm, seen in a fatal case of appendicitis reported by Robb.†

Warren Coleman,‡ in a man of sixty-seven, dead of nephritis and pneumonia, found in the dilated appendix a piece of bone five-eighths of an inch long and a quarter of an inch at its broadest part. It had entered blunt end foremost and was enveloped in mucus, completely filling the dilated tip. The thickened walls showed evidence of its presence for a long time, but externally there were no signs of inflammation. This case and that in which the appendix contained 122 shot, together with several that follow, show that, while generally causing very rapidly progressive inflammation, even large and rough foreign bodies can be present in the appendix and give no symptoms at all or can lead to chronic or recurrent appendicitis. Murphy§ also had an acute appendicitis, in which the offender was an enterolith having a spicule of bone as its nucleus. Thompson‖ reports a case in which a bone was present. Nathaniel Ward,¶ in 1855, had a patient who died after an acute illness of seven days. At autopsy it was seen that a small worn-down bristle from a tooth brush, a third of an inch long, had ulcerated through the base of the appendix and had given rise to purulent peritonitis. Dr. Schooler,** of Des Moines, removed an appendix containing a wisp of broom and another in which there was a bristle, and Abbe** recently had one containing a piece of corn husk.

In the Gynæcological Laboratory of the Johns Hopkins Hospital is a specimen (Fig. 3) which was successfully removed by Dr. W. E. Ashton†† from a woman forty-eight years old. She gave a history of abdominal pain, lasting through three years, and referred to the uterus which was curetted and the cervix amputated. The pain continued and increased, but did not become localized. Examination revealed nothing except a slight general soreness over the entire abdomen. An explor-

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* Stone and Ransohoff: Personal communication.

† Holmes: New England Quarterly Journal of Medicine and Surgery, Boston, 1882-3, I, 257.

‡ Hevin: Mémoires de l'Académie Royale de Chirurgie, 1743, I, 460.

§ Gibbons: West. Lancet, San Francisco, 1873, II, 113.

‖ Nelson: British American Journal of Medicine and Physical Science, Montreal, 1846-7, II, 257.

¶ Ulloa y Giralt: Revista mensual médico-quirúrgica de Neuva-York, 1878, I, 28.

** Blackadder: Edinburgh Medical and Surgical Journal, 1824, XXII, 18.

* Dr. Brower himself expects to publish this case *in extenso* at a later date.

† Robb: Johns Hopkins Hospital Bulletin, 1892, III, 23.

‡ Coleman: Medical Record, N. Y., 1895, XLVIII, 639.

§ Murphy: Journal of the American Medical Association, Chicago, 1894, XXII, 302.

‖ Thompson: British Medical Journal, Sept. 23d, 1892.

¶ Ward: Transactions of the Pathological Society of London, 1855, VI, 197.

** Schooler and Abbe: Personal communication.

†† Ashton: Medical Bulletin, Philadelphia, 1894, XVI, 85.



Fig. 1.—Appendix containing a round worm. Removed by Dr. C. F. Brower, Catharpin, Va. (By courtesy of Dr. Halsted.)

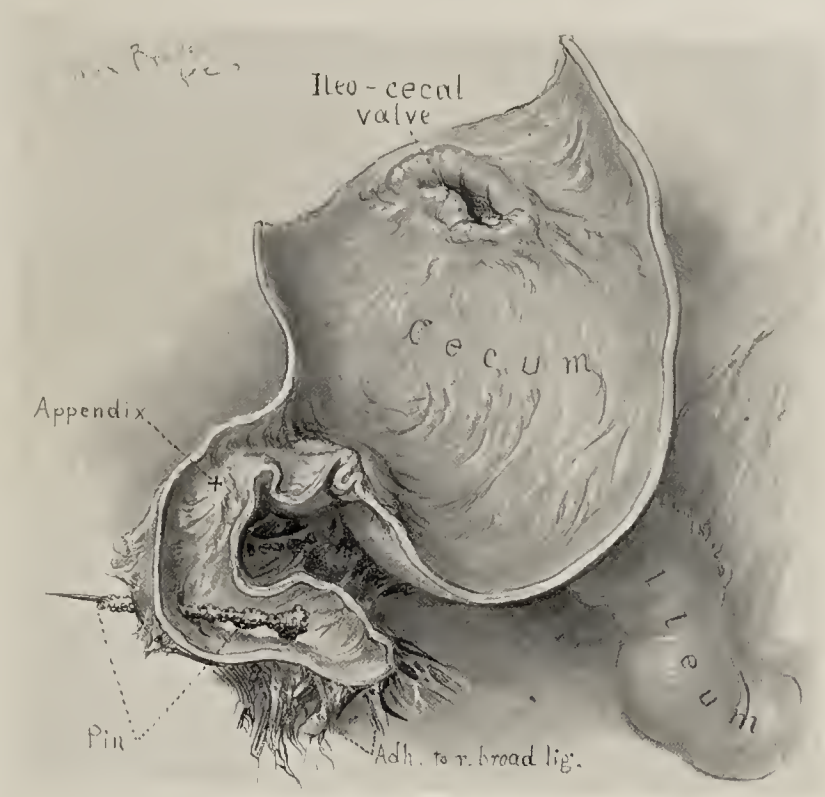


Fig. 2.—Appendix with pin perforating its wall. Removed by Dr. H. D. Rolleston, London, Eng. (Case 27.)



Fig. 3.—Appendix containing a fish fin. Removed by Dr. W. A. Ashton, Philadelphia.



Fig. 4.—Appendix containing three supposed gall-stones. Removed by Dr. W. R. Rogers, Memphis, Tenn.



Fig. 5.—Fæcal concretion with pin as nucleus. Removed by Dr. Francis H. Markoe, New York. (Case 10.)



Fig. 6.—Fæcal concretion with bullet as nucleus. Removed by Dr. Joseph Ransohoff, Cincinnati, O.

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atory abdominal incision was made, and the appendix, which was adherent to the brim of the pelvis, was removed. In it was the fin of a fish which, through pressure, had caused circulatory changes and ulceration.

PINS IN THE APPENDIX.

Conspicuous among pointed bodies and occurring with apparently greater frequency than any others are pins. Abbe,* in his large experience, has met with only two foreign bodies, and one of these a pin. Roswell Park† and McBurney‡ had each two cases, and numerous instances are to be found scattered through the literature. The earliest probable case we have encountered is described by Ruysch,§ of Amsterdam, in 1691. A young girl had swallowed a pin. Some time afterwards a hard inflammatory tumor appeared in the groin accompanied by fever and acute pain. Soothing applications having been used and suppuration induced, an incision was made in the tumor, and in the pus and fæcal matter evacuated was a rusty pin. ("Statim simul cum pure copioso acicula ærugino abducta prodit, non sine excrementorum alvinorum commixtione . . . . non est dubitandum, quin in principio, suborta inflammatione, intestinum, ab aciculæ mucrone læsum arctè connatum fuerit peritonæo.")

After a careful search we have collected twenty-eight other cases in which a pin was found in the appendix at operation or at autopsy, together with two instances in which a pin had perforated the cæcum.

In no single case has there been any knowledge of swallowing a pin and no explanation is offered for their presence.

Contrary to what might be expected, they occur more often in males than in females (males 17, females 9). Many are in of children under ten years of age; one in a boy of fifteen months; others in adults in various occupations and conditions of life.

One would naturally suppose that such a foreign body in the appendix would lead to rapid perforation; but, while this is generally the case, it is not always so. All types of appendicitis may result. Some give rise to only mild symptoms and may lead to chronic appendicitis (7 cases) with recurrent attacks, or with long-continued pain, or only a feeling of uneasiness in the right iliac region, which may last for months or years, and perhaps finally end in an abscess (Cases 14 and 15). Most often, however, there is rapid perforation and abscess formation following the first appearance of symptoms.

The pin may enter the appendix by its head or point. It is generally straight, lying in the lumen of the appendix with its long axis parallel to that of the appendix, and perforating with its point (Fig. 2). In one or two instances, however, it lay directly across the lumen and perforated with its head one wall, with its point the opposite. Dr. McBurney removed an appendix which contained two pins lying side by side and perforating the opposite walls of the appendix in this manner (Case 8).

On two occasions the pins have been found in appendices contained in hernial sacs.

The pin may be free from deposit, rusty or corroded. Usually, however, it is the nucleus of a fæcal concretion which covers the head and most of the shaft, leaving the point free. Such a body is shown in the accompanying cut (Fig. 5) from a case operated upon by Dr. Markoe (Case 10).

An interesting feature of this collection of cases is the frequent association of abscess of the liver, which was observed in seven of the twenty-eight.

From our investigation we can draw the following conclusions, supported by statistics:

Foreign bodies, at one time thought essential in appendicitis, are now known to play a much smaller rôle than that formerly accredited to them; and fæcal concretions are much more apt to be present as an exciting cause.

While many curious and unexpected things are occasionally found, the appendix nevertheless would seem to act especially as a trap for pointed bodies and for small heavy objects like shot or bullets.

Conspicuous among pointed bodies are pins, and their presence is by no means uncommon.

Those foreign bodies *of light weight*, like grape seeds and cherry stones, so popularly assigned as the cause of appendicitis, and against which we are forever being warned, are in reality exceptional, and their frequency is much overestimated on account of the close resemblance of fæcal concretions and the lack of careful examination of the bodies described.

The following cases, recorded in the literature and communicated privately, warrant the assertion that the pin is one of the commonest and at the same time the most dangerous of all foreign bodies.

CASES.

(1) *Mestivier* (1757): Jour. de Méd. Chir. Pharm., etc., 1759, X, 441.

A man, aged 45, presented himself with a large fluctuating tumor in the right side of abdomen near the umbilicus. It was opened and a pint of very foul pus evacuated. He died. At autopsy: "The cæcum presented nothing extraordinary. Here and there were gangrenous ulcers. Scarcely was the appendix opened, however, when there was found a large pin all encrusted and so eroded in places that the least force would have broken it."

Although the man had never mentioned swallowing a pin it was easy to conceive that it had long been shut up in the appendix, and by irritating the various coats had caused the trouble leading to death.

(2) *Parrot* (1855): Bull. Soc. anat. de Paris, 1855, 54.

Man, aged 24. Twelve years ago had pain in right inguinal region with the development of a tumor in the right iliac fossa. Eight years later the tumor made sudden progress. A year ago it was considerably increased and there were general symptoms and acute pains. An abscess opened and discharged considerable bloody pus. Patient was admitted with a fæcal fistula in lower right abdomen in which the probe encountered something hard. An incision was made and this body extracted with great difficulty. It proved to be an ordinary pin with the point free and otherwise enveloped in solid fæcal matter. The patient died with general peritonitis. Autopsy showed the fistula leading into a cavity into which opened the appendix.

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* Abbe: Personal communication.

† Park: Medical Record, New York, 1895, XLVII, 345.

‡ McBurney: Personal communication.

§ Ruysch: Observationum Anatomico-Chirurgicarum, Amsterdam, 1691, Observatio LV, 71.

Patient did not remember swallowing a pin.

(3) *Joffroy* (1869): Bull. Soc. anat. de Paris, 1869, XLIV, 512.

Girl, aged 10. Admitted with pain in right groin, radiating through abdomen, diarrhœa and incessant vomiting. Two days later tumor in right flank, which disappeared in a few days. Later, multiple superficial abscesses. Death in two months.

Autopsy: Circumscribed abscess in right iliac fossa with a collection of pus. In the appendix was found a pin of large size which had entered head first and had penetrated with its point the appendix wall. The pin was surrounded by fæcal matter.

(4) *Payne* (1870): Trans. Path. Soc., London, 1870, XXI, 231.

Woman, aged 37. Illness of three weeks; headache; abdominal pain; tenderness; bowels regular; temperature 104°; delirium and death.

Autopsy: Lodged in the appendix was a medium-sized black pin, the head and three-quarters of shaft surrounded by a fæcal concretion making a mass an inch long. The bare point of the pin projected into the cæcum. The appendix walls were thickened but there were no signs of acute inflammation. No general peritonitis. Abscesses of liver and lungs.

(5) *Legg* (1875): St. Barth. Hosp. Rep., London, 1875, XI, 85.

Girl, age 5. History of bronchitis, measles and scarlet fever, the last followed by an abscess in right groin which was poulticed and opened spontaneously. Child was well for a time and then wasted. Abscess developed in epigastrium; was opened, discharged great deal of pus; healed. Twelve days later abdominal distention, vomiting, death.

Autopsy: Multiple abscesses among intestines. Abscesses of liver. Appendix adherent to cæcum was cut across and a black pin was noticed which apparently came out of the gut; rusty on its head and upper third. On dissecting out the appendix, a round hole the size of a split pea and black around its edges was found to open from the appendix into peritoneal cavity close to cæcum.

(6) *Whipham* (1879): Trans. Clin. Soc., Lond., 1879, XII, 58.

Boy, aged 18. Five months before admission had an illness of six weeks; pain in side and diarrhœa. Seven days before admission pain in right side, shooting to axilla; next day bent with pain; sixth day vomiting, diarrhœa, abdominal tenderness; no tumor.

Operation: Incision; drainage tube in chest.

Few days later acute abdominal symptoms and death.

Autopsy: Localized abscess in right iliac fossa extending to sacrum and bladder; purulent and fæcal contents. Free in abscess cavity was a pin an inch and a half long. The appendix, doubled on itself, was perforated at opposite points in the fold. Appendix adherent to cæcum with a perforation into cæcum.

(7) *Ashby* (1879): Lancet, London, 1879, II, 649.

Girl, aged 8. Four months' illness; type of appendicitis. Pain in right side; legs drawn up; temperature 105°. Death.

Autopsy: Large abscess of liver. Appendix contained a pin encrusted with phosphates and its point sticking through appendix wall. Near this spot was a ragged ulcer with its base adherent to parts around.

No history of swallowing pin.

(8) *McBurney*, New York (1888): (Personal communication to Dr. Kelly.)

Boy, aged 10. Patient for some time had had what appeared to be an inflamed irreducible right inguinal hernia, the contents of which were thought to be omentum. At operation the contents were found to be a much-inflamed and thickened bulbous appendix, the enlarged distal end being about an inch in diameter. In this mass, the points piercing one side and the heads the other, were two black pins which lay close together. The appendix was amputated and the case finished as one of hernia. Recovery.

(9) *Baker* (1889): Brit. Med. Jour., 1889, 1347.

Man, with symptoms of intestinal obstruction and swelling in right iliac fossa.

Operation: Median incision and evacuation of fœtid pus. Six weeks later peritonitis and death.

Autopsy: A pin was found with its point protruding through the appendix, and its head buried in a mass of fæcal matter which could not be removed.

(10) *Francis N. Markoe*, New York (1892): (Personal communication to Dr. Kelly.)

Boy, aged 4. Child always well till four months ago. At that time had what his physician said was an acute attack of appendicitis, and an abscess was formed in the right iliac fossa, which opened spontaneously and left a discharging sinus. On admission there was found a sinus with several openings just below and to the inner side of the anterior superior spine. A probe passed an inch and a half downwards and backwards. Discharge had a fæcal odor.

Operation: Sinus curetted. No result. A few weeks later it was laid open, and a pin with a concretion about its middle was removed. No further attempt was made to explore the region. The appendix was not seen. After a short time the wound healed.

(11) *Shoemaker* (1892): Trans. Coll. Phys., Phila., 1892, 3 s., XIV, 214.

Male, aged 18. Illness of twelve days; chill; pain in right side; constipation; fæcal vomiting and subnormal temperature; abdomen tense and œdematous; no tumor; no jaundice.

Operation: Incision in the right semilunar line. General purulent peritonitis. Death next day.

Autopsy: General peritonitis. Ruptured hepatic abscess. Appendix not ruptured, but gangrenous and containing a common pin head downward.

(12) *Bell* (1894): Canada Med. Rec., November, 1894.

Boy, aged 6. Usual signs and symptoms of appendicitis. Two days' illness. Operation and recovery. On opening the appendix a pin was found lying transversely in its lumen, near the tip. The head of the pin had ulcerated through the wall of the appendix, and the point had nearly perforated the opposite side, and at this point the appendix was strengthened by a mass of adherent omentum.

(13) *Willard and Lloyd* (1894): Trans. Path. Soc. of Phila., 1894, XVII, 40.

Boy, aged 9. While under treatment for spinal caries developed acute abdominal symptoms; vomiting, abdominal pain and irregular temperature; legs drawn up; anxious expression.

Operation: Sixth day. Incision and drainage of abdominal abscess; collapse; death.

Autopsy: General peritonitis, with adhesions. Multiple abscesses of liver. Appendix perforated at a point near its base. Around this perforation were signs of inflammation. On laying appendix open it was found to contain a large black pin with its head toward the cul-de-sac, and its point projecting from the opening.

(14) *Park:* (1895): Med. Rec., N. Y., 1895, XLVII, 345.

Man, age 32. History of indefinite discomfort in right iliac fossa for five years, with acute attack of one week's duration.

Operation: Appendectomy. Extensive abscess. In appendix was a fæcal concretion three-quarters of an inch long and of the diameter of a lead pencil. Imbedded in it was a common pin with the point protruding. Drainage; recovery. Patient denied all knowledge of having swallowed a pin.

(15) *Park* (1895): Med. Rec., N. Y., 1895, XLVII, 345.

Girl, aged 15. Vague and indefinite discomfort for months in right iliac fossa. Finally symptoms of acute appendicitis with temperature and abdominal rigidity.

Operation: Incision parallel to Poupart's ligament. Three or four ounces of foul pus. Appendix not found, but a pin in the pus; drainage; recovery.

(16) *McPhedran and Craven* (1895): Canad. Pract., 1895, XX, 180.

Male, aged 21. Pain in abdomen and chest; temperature 103°; chills almost daily for six weeks; temperature sometimes reaching

106.4°. Aspiration of chest; no pus. Later, pus in ankle-joint. Four months later coughed up six ounces of pus. Pyuria. Death.

Autopsy: Small abscess of liver communicating with abscess in right pleural cavity, and this with a bronchus. Other liver abscesses. Appendix thickened and dilated. About its middle was a distinct cicatricial contraction and in the dilated extremity beyond lay a large-sized common pin. It was bent at an obtuse angle and its tip was imbedded for an eighth of an inch in the appendix wall. The pin was largely covered with a layer of calcareous matter laid down in a regular coat.

(17) *Colmer* (1895): Lancet, Lond., 1895, I, 745.

Boy, 7½ years of age. Three days' illness with vomiting, constipation and abdominal pain ending in sudden death. No history of swallowing a pin.

Autopsy: Signs of recent general peritonitis especially about the cæcum. Appendix thickened, enlarged and perforated, and through the perforation projected a sharp point. On opening the appendix there was found a body much like a date stone composed of fæcal matter enclosing a pin with the point projecting.

(18) *Abbe*, New York (1895): (Personal communication.)

Child, aged 5. Operation. Appendix had been perforated by a pin which had ulcerated out and was in an abscess cavity, of which the sloughing appendix was the centre. The pin was considerably encrusted with salts.

There was no history of the pin having been swallowed.

(19) *Kammerer* (1895): Annals of Surgery, 1895, XXII, 274.

Boy, aged 7. Illness of a week. Tumor in right side of abdomen.

Operation: Laparotomy. Tumor in omentum. On separating some adhesions it was found that the distal half of the appendix was firmly embedded in the mass, and that an ordinary pin had passed through almost the entire length of the appendix, and had escaped through a perforation at the tip. There were very firm adhesions of appendix to the omentum showing that this could not have been the first attack.

(20) *McBurney*, New York (1896): (Personal communication to Dr. Kelly.)

Man, aged 29. Five days before admission was suddenly taken with cramps in abdomen, general at first, but soon confined to right iliac fossa. Patient up and about; stoops to right to relieve pain. Tenderness over right iliac region. No tumor. Dulness over Poupart's ligament. Temperature 98°, pulse 80.

Operation: Incision over tumor, which was made out under ether and an ounce and a half of pus evacuated. In the abscess cavity a large soft concretion was felt. On attempting to remove it, it was found to be very friable and crumbled, showing an ordinary pin as the nucleus. The appendix had sloughed off near its base. Recovery.

(21) *Syms* (1896): Annals of Surgery, 1896, XXIII, 604.

Woman, aged 21. Good health till seven years ago, when she first had symptoms of appendicitis with a large abscess which opened spontaneously and healed. Repeated similar abscesses for six years. Finally a large abscess which was opened and drained. Second operation for persisting sinus showed tip of appendix attached to fascia under which was a cavity to which sinus led. In the appendix was found a toilet pin, the head of which was the nucleus of a hard fæcal concretion.

(22) *Roberts* (1896): Am. Pract. and News, Louisville, 1896, XXI, 491.

Boy, aged 15 months. Strong baby, bottle-fed. Illness of one day; vomiting; diarrhœa with bloody stools. After the last action a tumor appeared on right side of scrotum, which proved to be a strangulated hernia.

Operation: The cæcum with the appendix formed the hernial contents. On lifting up the appendix a pin was seen protruding from its posterior wall. It had passed through the sac into the dartos of the scrotum, the head being in the end of the appendix. Appendix removed and cæcum returned. Recovery.

(23) *Deaver* (1896): A Treatise on Appendicitis, 1896, 36.

Woman, aged 33. Ten days before operation sudden sharp pain in right side with vomiting for two days. Pain persisting for a week with tenderness and rigidity. Mass in right iliac fossa size of orange, not painful. Temperature 103°.

Operation: Appendectomy. No pus. Omentum adherent. Appendix contained a black pin which had entered the canal point first.

(24) *Daland* (1897): Proc. Path. Soc., Phil., 1897, n. s. I, 55.

Adult male. For a number of months pain in appendicial region. On admission typical symptoms of acute appendicitis of ten days' duration. Tenderness and rigidity.

Operation: Appendectomy. Eight ounces of pus evacuated from abscess cavity. Recovery.

An ordinary pin was found occupying the lumen of the appendix and, although causing no perforation, there were evidences of chronic appendicitis, shown by considerable thickening of the walls, partial encapsulation and presence of adhesions. The pin had become almost black in color.

No history of swallowing a pin.

(25) *Lee* (1897): Lancet, London, 1897, II, 536.

Woman, with history of sudden seizure with violent pain in abdomen. Death soon after.

Autopsy: A pin was found in the appendix, the point of which had evidently fretted its way through the end of the appendix. The opening thus made communicated with an abscess in the peritoneal cavity.

(26) *Officer* (1898): Intercol. Med. Jour., of Austral., 1898, 229.

Boy, aged 6. Ill nine days; headache; drowsiness; vomiting and fever; abdominal pain. No tumor. Two days later abdominal distention and legs drawn up.

Operation: Laparotomy. Peritoneal cavity full of pus. Irrigation and drainage. Death in 36 hours.

Autopsy: General peritonitis. Appendix found with difficulty, and on attempting to cut it out an ordinary pin was encountered, which had ulcerated through the wall of the appendix and was lying partly across its lumen.

(27) *Rolleston* (1898): Trans. Path. Soc., London, 1898, XLIX.

Girl, aged 7. Stitch in right side for a year or so. Five weeks before death signs of right pleurisy. Fever. Later, operation for abscess of liver with evacuation of pus. Death from asthenia.

Autopsy: Appendix adherent to broad ligament and surrounded by recent fibrinous peritonitis, appendix cut open, and at the point where it was so firmly adherent a pin was found with its head inside the tube, lying transversely to the long axis of the appendix. The shaft and tip of the pin after passing through the wall of the appendix were surrounded by old adhesions. The whole of the pin was irregularly encrusted with calcareous matter. Abscesses of liver.

(28) *Keen* (1898): Trans. of Am. Surgical Assoc., 1898.

Man, aged 24. When seven years old he had a great deal of trouble in passing urine, and when examined by the family physician, a pin was found well down in the urethra. He does not remember that he inserted it, and believes he swallowed it.

In March, 1896, it was supposed that a recto-vesical fistula was established following a prostatic abscess, and food was frequently recognized in the urine.

In April, 1897, after two unsuccessful operations for the closure of this fistula, laparotomy was finally performed. A long appendix was detected, the tip of which was solidly incorporated into the bladder, thus acting as a third ureter and discharging fæces instead of urine into the bladder. The appendix was separated from the bladder and removed, and the patient recovered, but later died of intestinal obstruction due to a volvulus.

The two cases which follow are so much like those under consideration as to deserve being included with them. In these the cæcum instead of the appendix was perforated by a pin, and the clinical picture was that of appendicitis.

(29) *Boussi* (1878): Bull. Soc. clin. de Paris, 1878, II, 15.

Woman, aged 40. Three weeks before admission, during and after menstruation violent abdominal pain and fever. Admitted with tumor in right iliac fossa, semi-fluctuant and tender; chills and vomiting. Death in sixteen days.

Autopsy: Abscess beneath liver communicating with abscess in right iliac fossa. In the pus was a blackened pin, which had perforated the cæcum.

Patient did not remember swallowing a pin.

(30) *Southam* (1898): British Medical Journal, Apr. 30, 1898, 1130.

Man, aged 29. Admitted with symptoms of acute appendicitis. Four days previously sudden pain in right iliac fossa with vomiting. On admission there was fulness above Poupart's ligament, tender and dull on percussion; rigidity of abdominal walls. Attack subsiding at end of a week. On ninth and tenth days fæcal vomiting.

Operation: Incision over appendix. An ounce of thick foul pus evacuated in which was a fæcal concretion, ovoid in shape and three-quarters of an inch long. In the centre of this was a pin with the head and point protruding. Drainage. Recovery with fæcal fistula.

At a second operation, three months later, there was found a fistulous opening in anterior wall of cæcum three inches from origin of appendix. Appendix perfectly healthy. Fistula sutured. Recovery.

Five additional cases have come to our notice too late to be included in the substance of this paper, which thus make thirty-three instances in which we have found a record of the presence of a pin in the vermiform appendix.

One is especially interesting, in that it is the only case in which there is any history of swallowing a pin.

Another makes an eighth instance of the association of liver abscess with appendicitis.

(31) *Robert P. Harris*, of Philadelphia, in a personal communication to Dr. Kelly recalls a case seen by Dr. Wm. Pepper, Sr., in consultation with Drs. Hugh Hodge and Meigs, where Dr. Pepper differed from his consultants and made a diagnosis of peritonitis. The woman died of peritonitis, and at the autopsy "a pin was found sticking through the end of the appendix, the cause of the peritonitis."

(32) *Harley* (Diseases of the Liver. London, 1883, 846):

Boy, aged 19. Admitted with fever; a rapid pulse, and tenderness over liver. Death in nine days.

Autopsy: Large abscess of liver. At the very apex of the appendix was a thick brass pin an inch and a quarter long, the head somewhat green and eroded, pointing downwards, and projecting through the caudal extremity of the appendix. A drop or two of pus was found outside of the peritoneum.

(33) *Schooler*, Des Moines, Iowa (1895): (Personal communication to Dr. Kelly.)

Man, aged 48. While pitching hay felt uneasiness in right side of abdomen, which later increased to pain. On second day a large tumor in the region of the appendix was made out. An incision was made and a quantity of pus escaped. Wound packed. On the third day the packing was removed and an opening seen in the bottom of the wound. The finger introduced in this felt a sharp point, which proved to be a pin, surrounded by pus. It was withdrawn with forceps. The appendix was not seen.

(34) *Schooler*, Des Moines, Iowa (1898): (Personal communication to Dr. Kelly.)

Girl, aged 2. Had been complaining for several days. Under anæsthesia a decided swelling was made out in the region of the appendix.

Operation: Incision into abscess. Evacuation of three ounces of pus. A pin was found sticking through the wall of the appendix, the head remaining inside. Appendix removed and wound packed. Recovery. The child had swallowed a pin several months before.

(35) *Harlow Brooks*, New York (1899): (Personal communication.)

Woman, aged 54. Illness of a week; headache and general pains; incontinence of urine and fæces. Diagnosis of "epidemic influenza, complicated by broncho-pneumonia." Death in ten days.

Autopsy: Diagnosis of broncho-pneumonia verified. The appendix was 8 cm. long; its tip dropped down into the pelvic cavity and was adherent to the right ovary which had become almost completely transformed into a cyst. Just at the centre of the appendix, where there were dense adhesions to the psoas muscle, there was a small cavity enclosed by the surrounding cicatricial tissue and containing pus and fæces. This abscess communicated with the lumen of the appendix. Lying in the proximal portion of the appendix, with its head at about the location of the abscess, was an ordinary pin encrusted with lime salts and fæcal matter. The pin lay with its head down, the shank extending up in the lumen of the appendix.

ORIGIN, DEVELOPMENT AND DEGENERATION OF THE BLOOD-VESSELS OF THE OVARY.*

(*From the Anatomical and Gynæcological Laboratories of the Johns Hopkins University.*)

PRELIMINARY STATEMENT.

AN ANATOMICAL AND PHYSIOLOGICAL STUDY OF THE VASCULAR SYSTEM OF THE OVARY AND ITS INFLUENCE UPON THE SUCCESSIVE STAGES AND ACCOMPANYING PHENOMENA OCCURRING IN THE EVOLUTION OF THE GRAAFIAN FOLLICLE. ALSO A CONSIDERATION OF THE RELATIONSHIP OF THE CORPUS LUTEUM TO THE CONSERVATION AND TO THE FINAL CESSATION OF OVULATION.

By J. G. Clark, M. D., *Late Resident Gynecologist in the Johns Hopkins Hospital, Associate in Gynæcology in the Johns Hopkins University.*

In February, 1896, at the suggestion of Prof. Mall, I began the study of the ovarian circulation, with a view of determining the normal distribution of the arteries and veins of the ovary and their relationship to each other. At first sight the solution of this question did not appear to present greater difficulties than those encountered in the ordinary course of any research. A study of the sections of a few injected adult ovaries, however, at once demonstrated the futility of attempting to draw any conclusion from this source, for the close crowding

* Presented before the Johns Hopkins Medical Society, December 19, 1898.

together of the parallel vessels of the medullary portion, and the markedly irregular course of those in the cortex or follicle-bearing zone, rendered impossible any accurate observations concerning the relative number and distribution of the veins and arteries, and the exact course followed by each system.

With a view, therefore, of securing ovaries possessing a simpler scheme, a study was made of the lower animals, such as the dog, rabbit, guinea-pig, sheep and pig, but with unsatisfactory results, and only after the injection of the generative organs of a monkey was a suggestive clue secured. Beyond this point, however, it was difficult to proceed, and only after the injection of a very large series of ovaries from individuals, ranging in age from a six-months fœtus to a woman many years beyond the menopause, were final conclusions reached.

In the search for this normal scheme through an extensive number of serial sections, various questions directly dependent upon the circulation have presented themselves for solution, which have widened the scope of this work until it has developed into a composite anatomical and physiological research.

Thus the various vital phenomena have been considered which transpire within the follicle from its embryological origin and progressive growth to the time of its disappearance, either through an obliterative process or through its rupture, organization as a corpus luteum and final retrogression as a corpus fibrosum. In this connection theories have been suggested as to the cause of ovulation, the synchronism of ovulation and menstruation, the mechanism of the rupture of the mature follicle and the final cessation of ovulation, which have been based upon observations made in the study of a very large number of sections.

Soon after beginning this work I was struck not only with the difficulty of arriving at a definite knowledge of the scheme, but also of determining the age at which this scheme may be taken as a standard for comparison.

This is certainly not possible after active ovulation is established for the constant changes in the vascular system induced through the maturation, rupture and organization of the follicle, introduce an element of variability into the circulation of this organ which, so far as I know, occurs in no other.

Failing to reach any satisfactory starting point in the adult, the ovary of a girl approaching puberty was next studied, but with little less success, for it was found that almost as constant variations occur in the follicular circulation before as after the inauguration of ovulation. In the hope of finally reaching a period in the life of the female individual, at which a definite standard for comparison might be found, numerous specimens from children of various ages were injected and closely studied. Finally the ovary of a six-months fœtus was obtained, which furnished a definite clew as to the arrangement of the vessels, but as the follicular apparatus was still in process of development a new-born child in which the tunica albuginea was well formed was selected as the standard. Even here the solution of the question was not easy, for in order to trace the ramifications of the vessels from the point of their entrance into the ovary to their ultimate termini the study of the serial sections of many ovaries was necessary.

To briefly summarize the chief points in this investigation I have considered them under a skeleton outline, the main headings of which will conform in general to the arrangement in my forthcoming paper.

In this preliminary statement it is impossible to more than hint at the points which will, in the final publication, be developed through schematic demonstrations and many drawings from injected specimens, and for the same reason references to the numerous researches which have been made upon many of the subjects considered in this report must be omitted.

EMBRYOLOGICAL CONSIDERATIONS.

The primitive circulation of the Wolffian body will be dwelt upon, and an explanation of the origin of the spermatic vessels as an independent system from that of the former will be offered. As is well known among embryologists the Wolffian and Müllerian ducts are well formed and the germinal eminence is of considerable size before visible signs of the differentiation of sex become manifest. Up to this point the embryo is said to be of the hermaphroditic or indifferent type.

In retracing the steps of development from the well-formed embryo back to this period some very interesting points concerning the differentiation of sex have been secured. The radical differences existing between the vascular system of the testicle and ovary have furnished a valuable sign for determining the gender of very young embryos, before the external differential marks are established.

The fact to which attention will be directed especially is that the testicular circulation is peripheral, the main artery of which courses over the dorsal aspect of the organ, giving off in its course rib-like branches which in turn send penetrating branches into the gland. Between the arteries are situated the collecting veins which unite at the base of the testicle to form the spermatic plexus.

In the ovary this scheme is exactly reversed, the arteries with their accompanying veins entering the center of the organ where they branch tree-like and terminate as a fine capillary anastomosis in the tunica albuginea.

Upon the peculiarities of each circulation the differential signs of sex are based—a visible dorsal vessel always indicating a male; an alabastic-like non-vascular white cortex a female embryo.

In microscopic sections the presence of large peripheral vessels also indicates the male, whereas large central vessels indicate the female sex.

The significance of the vascular arrangements in the testicle and ovary will also be discussed from the physiological standpoint, and to the radical differences existing between them will be ascribed the persistence of the testicular function in the male to old age, and the comparatively early abrogation of ovulation in the female. In the testicle the production of sperma is a more or less fixed and constant function like that of the pancreas, the parotid and other secreting glands, consequently the circulation is not subject to variations and is only interrupted through disease or through senile changes, whereas in the ovary there is a constant variation in the circulation incident to the obliteration or disappearance of follicles and the compensatory production of connective tissue which sooner or

later begins to limit the peripheral circulation, and this in turn leads though secondary influences to a final cessation of ovulation.

Incidentally, I may remark that these wide differences in the circulation lead me to the conclusion that the origins of the ovary and testicle are not as generally believed the same, but are totally different, and that the expressions "asexual period," "hermaphroditic stage of the embryo," etc., merely serve to mask our inability to select the differential features of the sexes back of this point.

In view of the fact that the common progenitor of the ovary and testicle is the Wolffian body and that the atrophy or degeneration of the latter is coincident with the active growth of the former, an endeavor has been made to discover the explanation of this apparent paradox. According to my observations upon this point, it lies in the fact that the vascular system of the sexual glands originates entirely independently of that of the Wolffian body, consequently the synchronous development and degeneration of the two sets of organs is possible.

Having traced the development of the circulation in the ovary and testicle from the so-called asexual period to the point where they have formed systems diametrically opposite in their distribution and ultimate arrangement, the further consideration of the testicle will be dropped and the study of the ovary along the line of its development and progression to its ultimate history will be pursued.

Development of the Graafian Follicle.

My study leads me to reject the Valentine–Pflüger theory concerning the origin of the follicle and to accept, with some reservation, the general scheme of development as suggested by Waldeyer. So far as the genesis of the "egg nests" and their ultimate subdivision into follicles are concerned, I am in accord with the latter investigator, but as to the origin of the so-called follicle epithelium or membrana granulosa, I feel that the evidence in my hands is sufficient to put me at variance with Waldeyer's conception and to incline me towards that of Foulis, who believes that the germinal epithelium only forms ova and that the lining membrane of the follicle is derived from the connective tissue stroma.

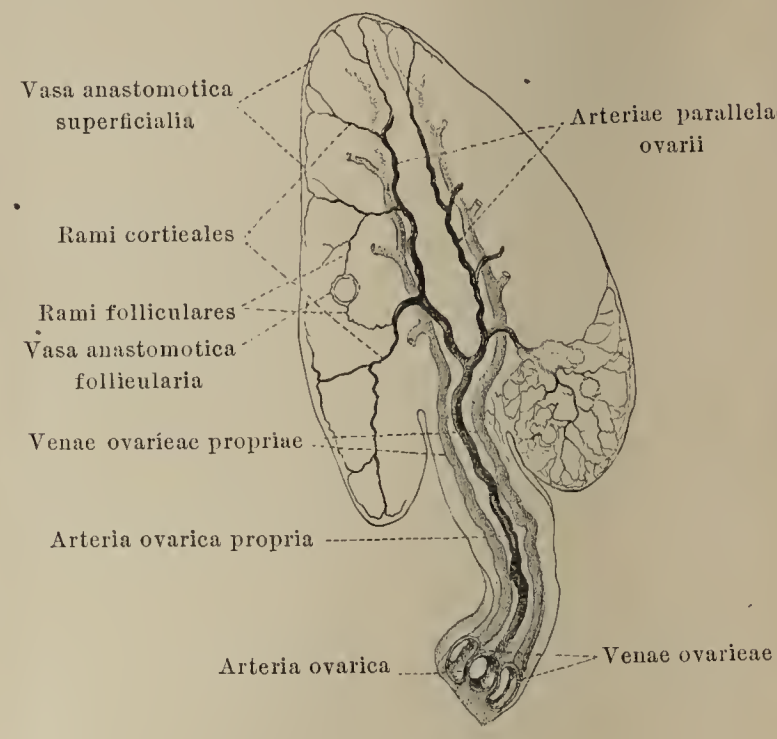
The Ovarian Circulation of the New-Born Child.

With the completion of the fibrous covering of the ovary (tunica albuginea) shortly after birth, the vascular system becomes fully developed, and this period, therefore, may be said to represent the typical scheme, for up to this point there has been no derangement of its central or peripheral branches, which will occur later through the progressive development and degeneration of follicles.

The secondary branches of the circulatory tree occupy a comparatively small medullary area, its tertiary branches being given directly off into the follicle-bearing zone. The follicles are, as as rule, still in their primitive state, only a few of the many thousands as yet showing progressive development.

Even at this early period, however, isolated follicles undergoing progressive and retrogressive changes may be noted. These changes, as I shall hope to show, are closely analogous to if not identical with those occurring in the ovaries of older children, and in women after ovulation is inaugurated.

The arrangement of the circulation as established at this early age is shown in the following schematic way:



As will be seen from this sketch each follicle is provided with a vascular wreath, which is formed by the terminal twigs of the main cortical branches.

The development of this wreath and its final obliteration, along with the disappearance of the corpus luteum, does not affect the general scheme, for it merely represents one small terminal system, the destruction of which, so far as its effect upon the general system is concerned, is like the lopping off of an ultimate twig of the branch of a large tree.

For this reason the changes in the ovarian circulation incident to the progressive development and degeneration of the follicles, even in early womanhood, are local and not general. It is only in the later periods of the ovulating life of the female that the latter effect is noted. Beyond the follicular zone the terminal vessels break up into capillaries which form a fine parallel running anastomosis in the tunica albuginea, which hitherto has not been described.

The extensive anastomosis throughout the ovary renders easy the shifting of the circulation from one set of vessels to another, consequently the destruction of the function of the ovary is almost an impossibility before its final cessation through natural causes.

In the same way the persistence of the function in even tiny bits of the ovary, which are occasionally left after an ovariotomy, may be explained.

In order to conform to the new method of classification, recently decided upon by anatomists, a system of nomenclature has been adopted which is based upon the regional distribution of the vessels.

CLASSIFICATION OF VESSELS:

ENGLISH.	LATIN.
varian artery.	Arteria ovarica.
" veins.	Venæ ovaricæ or Vv. ovaricæ.
xtra ovarian or hilus branch of artery.	Arteria ovarica propria or Aa. ovaricæ propriæ (Ramus I, II, III, IV, V).
xtra ov., or hilus branches of veins.	Venæ ovaricæ propriæ.
edullary branches.	Rami medullares or arteriæ parallelæ ovarii.
ortical branches.	Rami corticales.
eripheral anastomosis.	Vasa capillaria anastomotica superficialia.
ollicular branches.	Rami folliculares.
" anastomosis.	Vasa anastomotica follicularia.
tero-ovarian anastomosis.	Arteria anastomotica uterina.

In order to follow the progressive changes in the ovary from irth to the climacteric, specimens from my collection repre-nting the following ages have been selected: child of 2 years, rls of 9 and 12 years, and of 14 years, just after the establish-ent of ovulation, young woman of 24 years, middle-aged oman of 35 years, woman approaching the menopause at 42 ars, and finally an old woman of 66 years, long after the enopause.

In these specimens an endeavor has been made to follow not ly the changes incident to the circulatory system, but also e other progressive histological transformations.

The comparison of this ascending series has suggested rtain hypotheses concerning the physiology of the ovary, hich I trust have been strongly sustained, if not confirmed, the specimens in hand.

THE OVARY OF A CHILD OF TWO YEARS.

In the six-months fœtus the main branches of the ovarian tery correspond in the general form of their distribution to e fasciculi of a widely spread folding-fan, the divisions tween the arteries being filled with primitive follicles.

As the ovary grows in age the vessels with the connective sue septæ, which form these divisions, change from a gently rved to a perpendicular course, the branches occupying the edullary portion being crowded into parallel lines (arteriæ rallelæ ovarii).

In the two year old child, through the development and rogression of numerous follicles from birth up to this time, e medullary area comprises a much larger portion of the ary than that noted in the new-born.

As there is no increase in the number of follicles after birth e obliteration of each primitive or partially developed one turally decreases the total original number, which results in increase in the medullary portion of the ovary at the expense the follicle-bearing or cortical zone.

The law of development in the follicle is from within ward, that is the primitive follicles lying nearest the ntral circulatory tree are the first to undergo development.

In the young child the developing follicles instead of moving towards the periphery, as occurs in the girl approaching puberty or in the adult, tend to maintain their primitive position, their enlargement being simply centripetal without any attempt at mobilization.

Having reached a certain stage in their development, a retrogressive change following the degeneration of the ovum is inaugurated, and the original site, occupied by the follicle, is replaced by a very minute addition of connective tissue to the stroma of the organ, which naturally builds up through successive accumulations the central area.

Follicles in various stages of development and retrogression are noted in all ages after birth, and according to my observations the same principle involved in the obliteration of the unruptured follicles before puberty governs the organization of the corpus luteum after ovulation is inaugurated.

Briefly stated the changes consist in an increase in the vascular wreath around the primitive follicle and a coincident or dependent hyperplasia of the membrana propria and an accumulation of liquor folliculi.

What determines the cessation of these progressive changes and the beginning of the retrogressive or obliterative process remains unexplained. The fact remains, however, that with the degeneration of the ovum the liquor folliculi is absorbed and the cavity is filled in with large embryonic connective tissue cells arising from the theca interna.

Through the gradual diminution in the blood supplied by the follicular wreath the excess of connective tissue undergoes hyaline changes and absorption until finally only a mere trace of the new-growth remains.

In this way the size of the ovary is maintained within reasonable bounds. Were each mature or large follicle to be replaced by permanent connective tissue, the ovary would very early in life assume the proportions of a new-growth, which sooner or later would constitute fibromata of no mean dimensions.

PROGRESSIVE CHANGES IN THE OVARY.

In the progressive growth of the ovary the obliterative changes just referred to continue until the follicle-bearing area, reduced by many thousands in its numbers of primitive follicles, becomes a narrow zone compared with its width in the new-born child.

The crowding together in more or less parallel lines of the secondary and tertiary branches of the ovarian vessels is, to return to our analogy, simulated by the partial closure of the fasciculi of the fan. The increase in the internal resistance through the building up of a denser medullary centre and the closer crowding together of the parallel vessels sooner or later breaks the equilibrium of forces and consequently the follicles no longer maintain their primitive position while enlarging but undergo mobilization towards the tunica albuginea, that being the direction of least resistance.

The actual rupture of the follicle, according to my opinion, is due to the influx of blood during the menstrual cycle into the medullary blood-vessels, which has a double action, first to push the mature follicle rapidly towards the surface, and

second, through the increased pressure, to close the parallel running anastomosis in the tunica albuginea, and thus permit a physiological necrosis and rupture of the follicle.

Concerning the question of ovulation and menstruation I shall endeavor to offer further evidence to prove that the rule of synchronism is the normal, and that deviations from this rule are probably due to modifications in the life habit incident to changes in environment and to departures from primitive methods of living and from primitive laws governing sexual congress.

A brief paragraph will be devoted to the processes through which the mature but unruptured follicles undergo obliteration. I shall assume that this is not a pathological condition, but is merely Nature's method of getting rid of a functionless cavity. The organization of the vascular system of the corpus luteum, followed by its retrogressive changes and final disappearance, will be considered, and I shall take the position that little or nothing of the follicular vascular system remains when the resorption of the corpora fibrosa is complete.

As a conclusion to this study the cessation of ovulation will be ascribed to the gradual impairment of the vascular systems, through first, densification of the ovarian stroma and second, through the retroactive effect of imperfectly removed corpora lutea, which as an end result diminishes the blood-supply to the cortical area to such an extent that the growth of the primitive follicles is retarded and finally completely inhibited. These final retrogressive changes lead up to and constitute the menopause or climaterium.

OVARIAN CYSTS IN THE NEGRESS.

By Thomas R. Brown, M. D.

Comparatively little has been written concerning ovarian cysts in the negress, probably partly because that in most hospitals where extensive gynecological operations are performed the proportion of negro patients is very small, and partly because of the comparative rarity of this condition in negro women.

In fact, one frequently hears surgeons say: "The tumor before us presents all the features of an ovarian cyst, but inasmuch as the patient is a negress it is certainly not so, but a tumor of different origin (cystic myoma, etc.), as multilocular cysts are unknown in the negress."

That ovarian cysts are much rarer in negresses than in white women no one will deny, but as to the exact numerical relationship between the two few if any figures of importance are obtainable, and the object of this note is to give definitely and numerically this proportion as obtained by an analysis of ovarian cysts of various kinds operated upon at the Johns Hopkins Hospital.

In considering ovarian cysts the usual divisions have been made into (*a*) simple retention cysts, including Graafian follicle and corpus luteum cysts; (*b*) unilocular and multilocular ovarian cystomata, the two being considered together, as many regard the unilocular cysts as originally multilocular; (*c*) papillary cysts and (*d*) dermoid cysts of the ovary; also for sake of completeness parovarian cysts and intraligamentary cysts have been considered.

I shall discuss the frequency of ovarian cysts in the negress first (I) from a clinical and macroscopical standpoint, and second (II) from a microscopical and pathological standpoint, which is much more important.

I.

An analysis is here given of the various kinds of ovarian cysts occurring in the white and the colored for a period of six years, from January 31st, 1892, until January 31st, 1898, the variety of cyst being determined by clinical observation and macroscopic appearance.

Total No. of cases of all kinds treated in the gynecological service.		VARIETIES OF CYSTS.											
		Dermoid cysts.		Simple cysts (Graafian follicle and corpus luteum cysts).		Unilocular and multilocular cysts.		Papillary cysts.		Parovarian cysts.		Intraligamentary cysts.	
Wh.	Col.	Wh.	Col.	Wh.	Col.	Wh.	Col.	Wh.	Col.	Wh.	Col.	Wh.	Col.
3996	589	17	7	88	3	53	2	14	0	4	0	3	0

It will thus be seen that out of 191 cysts, only 12 were in the negress, a proportion of 1 : 15, while the proportion of colored to white gynecological patients treated during the same period was 1 : 6.75 (589 : 3996), *i. e.* ovarian cysts were relatively 2.2 times as frequent in white as compared with colored women.

When we analyze the proportion in the different varieties of cysts, we arrive at some striking results.

In the case of the dermoid cysts, cysts due to the inclusion of some of the embryonic ectoderm in the ovarian tissue, we find that 7 of the 24 cases reported were in the negress, *i. e.* 1 : 2.5 (7 : 17), which would seem to indicate that the dermoid cysts are relatively more than twice as common in the negress as in the white woman (the proportion of white to colored gynecological patients being 1 : 6.75).

As regards simple retention cysts, the proportion of 3 to 88 (*i. e.* 1 : 29.3) is probably not a fair estimate, due to the fact that what to call a Graafian follicle cyst and what to call a dilated Graafian follicle depends largely upon the individual operator.

When we consider unilocular and multilocular cysts, however, we are struck at once by their remarkable infrequency in the negress, of the 55 cases mentioned only 2 being in that race, *i. e.* a proportion of 1 : 26.5.

This is of especial importance, because this form of cyst of the ovary grows to the largest size, and it is this variety of cyst which many surgeons declare never occurs in the negress.

No cases were reported of papillary cysts of the ovary, parovarian or intraligamentary cysts in the negress.

Thus it will be seen that with the exception of dermoid cysts, ovarian cysts are really much less common in the colored race, the results, however, being more or less indefinite, due to the fact that the diagnosis was made clinically and macroscopically and not microscopically.

II.

An analysis of ovarian cysts from the microscopical standpoint was made from all cases operated upon in the Hospital from the latter part of 1893 until October, 1898.

During that time there had been microscopically described and diagnosed in the Gynecological-Pathological Laboratory 244 ovarian and parovarian cysts, divided as follows: Dermoid cysts 32, Graafian follicle cysts 68, corpus luteum cysts 16, unilocular and multilocular cysts 94, papillary cysts 10, and parovarian cysts 24.

(*a*) Dermoid cysts. Of the 32 dermoid cysts, 6 were in the colored, *i. e.* the proportion is 1 : 4.3, showing, as in the clinical study above, that these cysts are relatively more common in the negro race.

CASES OF DERMOID CYST OF THE OVARY IN THE COLORED.

CASES.	PATHOLOGICAL REPORT.	REMARKS.
(1) S.	Dermoid cyst of right ovary, 7 cm. in diameter	
(2) J.	Dermoid cyst of ovary, 16 cm. in diameter	
(3) I.	Dermoid cyst of ovary, 7 cm. in diameter	Myomatous uterus.
(4) S.	Dermoid cyst of ovary, 8 cm. in diameter	
(5) V.	Dermoid cyst of ovary, 4.5x3.5x3 cm	2 intraligamentary myomata.
(6) C.	Dermoid cyst of right ovary, 2.5 cm. in diameter.....	Myomata uteri.

(*b*) Retention cysts. Of the 84 simple retention cysts (68 Graafian follicle cysts, 16 corpus luteum cysts), 7 were in the colored, a proportion of 1 : 11, showing that these cysts are relativcly less common in the negress than in the white woman (as stated before, the proportion of colored to white gynecological patients being 1 : 6.75).

CASES OF SIMPLE RETENTION CYSTS IN THE COLORED.

CASES.	PATHOLOGICAL REPORT.	REMARKS.
(1) S.	Right unilocular ovarian cyst, probably dilated Graafian follicle, intraligamentary, 9 cm. in diameter.	Double pyosalpinx.
(2) C.	Right corpus luteum cyst, 5 cm. in diameter.	Epithelioma of cervix.
(3) W.	Cyst of ovary from corpus luteum or Graafian follicle, 6x4x4.5 cm.	Double perisalpingitis and perioöphoritis.
(4) W.	Corpus luteum cyst, unilocular, 5 cm. in diameter.	
(5) B.	Cyst of left ovary, 5 cm. in diameter (probably of Graafian follicle).	Myomata uteri.
(6) B.	Graafian follicle cyst of right ovary, 4 cm. in diameter.	Myomata uteri.
(7) T.	Right Graafian follicle cyst, 4x3 cm.	

(*c*) Unilocular and multilocular cysts. Of the 94 unilocular and multilocular ovarian cysts, but 6 were in the colored, the proportion thus being but 1 : 14.7, showing that this form of cyst is relatively more than twice as common amongst white women.

It shows, however, that they are by no means so uncommon in the negress as popularly supposed.

CASES OF UNILOCULAR AND MULTILOCULAR OVARIAN CYSTS IN THE COLORED.

(1) G.—Color, black.

Pathological Report.—Multilocular ovarian cyst. Myoma uteri.

(2) H.—Color, black.

Examination.—Abdomen, especially right side, is distended by a firm elastic tumor mass reaching 9 cm. above the umbilicus, its longest axis being 23 cm. In left inguinal region is felt a hard, irregular mass, the size of a small hen egg.

Operation.—Cystectomy. Hystero-myo-salpingo-oöphorectomy.

The cyst was thin-walled, filled with bloody fluid; it was developed from the outer pole of the right ovary and was entirely retroperitoneal. The uterus was myomatous, and there were many adhesions, especially about the cyst.

Pathological Report.—Multilocular cyst of right ovary 16 cm. in diameter, springing from the upper pole; the cyst wall is 1 mm. thick, the fluid is dark reddish-chocolate colored. Myomata uteri.

(3) I.—Color, black.

Examination.—Abdomen is much distended in its lower half, and a large mass of irregular outline can be palpated; to the right it feels elastic; to the left hard. The upper border of the mass reaches in the right parasternal line to within 11 cm. of the costal margin. Transversely it measures 29 cm.

Operation.—Cystectomy. Hystero-myo-salpingo-oöphorectomy.

On the right side a multilocular ovarian cyst posterior to the uterus, filling the cul-de-sac and rising above the pelvic brim, with its walls intimately adherent to the intestines. Myomatous uterus, size of fœtal head.

Pathological Report.—Ovarian cyst (either multi- or unilocular, probably the latter); fluid is clear, limpid and yellowish. Myomata uteri.

(4) C.—Color, black.

Examination.—Abdomen is irregularly distended. On palpation a mass, divisible into two separate masses, can be made out, one occupying the lower portion of the abdomen, with irregular outline and nodular surface, the other reaching as high as the costal margin on the left, measuring 9x12½ cm. with smooth surface and elastic feel.

Operation.—Hystero-myomectomy. Cystectomy.

The cyst was punctured and the fluid withdrawn before the enucleation was started.

Pathological Report.—Left unilocular ovarian cyst, 7 cm. in diameter.

(5) F.—Color, black.

Examination.—The body of the uterus is apparently of normal size and is pressed backwards by a large abdominal tumor, which is firm, elastic, tense, of smooth surface and gives a distinct wave of fluctuation. Corona of resonance is well marked.

Operation.—Cystectomy (left). Right salpingo-oöphorectomy.

The cyst-wall was punctured, the fluid obtained therefrom being of a muddy brown color. The cyst sprang from the left ovary and was adherent to the omentum. The right tube and broad ligament were plastered over the surface of the cyst. Right salpingitis. The uterus contained a few myomatous nodules.

Pathological Report.—Large multilocular cyst of left ovary, 19x18 cm., containing 1800 c. cm. of dark brown fluid containing much albumen.

(6) H.—Color, black.

Pathological Report.—Right multilocular ovarian cyst, 6 cm. in diameter, dense adhesions, cyst of left ovary 5 cm. in diameter, containing blood and débris.

Thus it will be seen that, although these cysts are less common in the negro race, nevertheless they do sometimes occur, and reach as large a size in some cases as the corresponding cysts in the white race, and thus the possibility of their being present should always be seriously considered when the physical examination points in that direction.

(*d*) Papillary cysts. No case of this kind was found in the negress in the cases analyzed.

(*e*) Parovarian cysts. Of the 24 parovarian cysts, only 1 was in the negress, showing the extreme rarity of this variety of cyst in this race.

(1) A.—*Pathological Report.* Right parovarian cyst. Myoma uteri. Left salpingitis.

Thus, of the 244 cases of ovarian and parovarian cysts, but 20 were in the colored race, *i. e.* the proportion is 1 : 11.2, showing that the relative frequency of these cysts is 1.66 times as great in the white as in the colored race.

If we exclude the parovarian cysts, of the remaining 220 true ovarian cysts 19 were in the negress, a proportion of 1 : 10.6, *i. e.* the relative frequency is 1.57 times as great in the white as in the colored race.

If we exclude the dermoid cysts, cysts which owe their origin to some defect in embryonic development, of the remaining 188 ovarian cysts (corpus luteum, Graafian follicle, multilocular, unilocular and papillary cysts), but 13 were in the colored, *i. e.* a proportion of 1 : 13.4, showing that these cysts are *relatively* exactly twice as frequent in white women as in colored.

Perhaps the thing that strikes one most in studying these cases is the extreme frequency with which the ovarian cysts in the colored are associated with other pathological conditions, especially with a myomatous condition of the uterus.

In 10 of the 20 cases reported, uterine myomata were also found. These were distributed as follows: In 3 of the 6 cases of dermoid cysts; 2 of the 7 cases of Graafian follicle and corpus luteum cysts; 4 of the 6 cases of unilocular and multilocular cysts; and in the 1 case of parovarian cyst reported.

In 3 of the 20 cases salpingitis, perisalpingitis or pyosalpinx was reported, *i. e.* evidences of inflammatory trouble, distributed as follows: In 2 of the 7 cases of corpus luteum and Graafian follicle cysts, and in the 1 case of parovarian cyst.

Thus, to summarize our results, while the simple retention cysts and the unilocular and multilocular ovarian cysts are seen relatively much less frequently in the negress than in the white woman, they are present relatively much more frequently than is universally supposed; while from both a clinical and pathological study the dermoid ovarian cyst seems to be relatively more frequent in the negro race.

ON A HITHERTO UNDESCRIBED PEPTONISING DIPLOCOCCUS CAUSING ACUTE ULCERATIVE ENDOCARDITIS.

(PRELIMINARY REPORT.)

By W. G. MacCallum, M. D., and T. W. Hastings, M. D.

(*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*)

A. S., aged 37, was admitted to the service of Dr. Osler, September 14, 1898. Occupation and family history unimportant; personal history negative, excepting for an account of an indefinite febrile attack of three weeks' duration, in 1889, which was said to have been rheumatic fever.

Since July 4th, after contracting a severe cold, he had a fever which had been persistent until early in August, when it subsided but reappeared about the middle of the same month, and for this supposed relapse of typhoid fever the patient was sent to the hospital.

The signs of aortic valvular disease were noted on admission and the diagnosis of septicæmia and probable malignant endocarditis affecting the aortic valves was made after obtaining positive blood cultures on September 24th.

The growth from the blood cultures was thought to be a short-chained streptococcus often occurring in pairs, but subsequently, on study of that obtained upon different media, it proved to be a definite diplococcus. On October 1st, three days before death, blood cultures were taken a second time from the basilic vein with the same positive result.

The autopsy revealed an acute vegetative and ulcerative aortic and mitral endocarditis. The aortic valves were bound together by exuberant branching vegetations which had undergone ulceration; several of the mitral chordæ tendineæ were ruptured and the broken ends covered with vegetations. In the spleen and kidney there were septic infarctions in various stages of softening, the fresher ones being firm and white, the oldest forming large thin-walled cavities with almost diffluent contents. One such embolic abscess was found in the ileum. There was also a bronchopneumonia of the left lung.

Sections of the aortic valves showed the fibrinous vegetations to be loaded with masses of diplococci, and in those passing through the infarcts in the kidney plugs of similar cocci were found in the vessels at the edges of the infarcted area. From the heart's blood and the aortic vegetations, as well as the infarcts in the spleen and kidney and from the lung, pure cultures were obtained of the diplococcus which presented, in brief, the following morphological and biological characters:

Morphology.—A small somewhat elongated diplococcus occurring sometimes in chains of four, but generally in pairs,

which stained easily by methods of Gram and Weigert. No demonstrable capsule.

Agar Growths showed minute semi-translucent pin-point deep colonies and corresponding minute discrete translucent round superficial colonies. On slant agar the smear gave rise to a thin translucent growth made up of conglomerated colonies, the edge of which is slightly raised and crenated.

Glucose and ascitic fluid agar afforded a more profuse and rather less translucent growth, while on glycerine agar the growth was comparatively scanty. There was no gas formation in glucose agar.

Potato.—The growth was slow to appear; after two or three days it showed as a dry whitish or tawny layer.

Bouillon was rendered very slightly opalescent after forty-eight hours.

Litmus-milk was decolorized within four hours. Later (within forty-eight hours) the milk was coagulated and acidified. After this there was a rapid peptonization of the coagulum, the medium becoming transformed first into a turbid purplish fluid, or a turbid yellow fluid, overlaid by a layer of red, and later into a quite clear blood-red fluid. This reaction is very characteristic and absolutely constant.

Blood Serum.—The growth appeared in minute discrete dew-like colonies. Within forty-eight hours there appeared a depression on the surface of the medium corresponding with the line of smear. Liquefaction of the medium occurred in course of time.

Gelatin was rather slowly but completely liquefied. Stab cultures took on the appearance of a wide funnel after about four days.

The sediment of organisms like the colonies on gelatin plates had a pale sulphur-yellow color.

The organism is quite hardy and may be recultivated from tubes several weeks old.

Anaërobiosis.—It is a facultative anaërobe, cultures in Buchner jars growing with about the same profusion and rapidity as the aërobic controls. In an atmosphere of hydrogen the growth is rather less abundant.

Thermal Death Point.—The diplococcus is killed in five minutes by a temperature ranging between 60° and 65° C.

Pathogenicity.—Laboratory animals succumb to inoculation. White mice do not survive the intraperitoneal injection of suspension of the cultures. Death may take place as early as eight hours or be delayed for three or four days. The microorganism can be recovered from the blood and organs generally.

The subcutaneous inoculations of mice also produce fatal effects after a longer period—two to four days. In the latter positive experiments no lesion was found at the point of inoculation and the organism was not recovered from any source.

Rabbits appeared less susceptible. Of several experiments one rabbit which received 3 cc. of a suspension of the organism intravenously succumbed in 16 days. At the autopsy there was found an abscess at the site of inoculation, and from this as well as from the distended urinary bladder the organism was recovered.

One dog has thus far been inoculated after injury of the aortic valves by the passage of a probe into the heart through the carotid (Rosenbach's operation), the culture being thrown into a vein. After five days the dog was killed and the autopsy revealed a fresh vegetative endocarditis, the vegetations springing from the edges of the perforation in the valve and from the point on the aortic wall where the intima was scraped off by the probe. There was also an extension of the vegetations onto the mitral valve; and at the point where the probe passed into the intraventricular septum an acute suppurative myocarditis had formed. The organism was recovered in pure culture from the aortic vegetations and from the heart's blood and organs generally.

Experiments with the ferments and toxines are in progress and will be reported later.

This diplococcus which has been proven to be pathogenic for man and some of the lower animals seems not to have been met with before—at least, there is no record of such an organism to be found in the bacteriological literature available to us. The chief peculiarities which distinguish it from the pyogenic cocci already described are:

(1) The mode of growth which resembles that of the micrococcus lanceolatus, the diplococcus intracellularis meningitidis and the streptococcus rather than that of the pyogenic staphylococci.

(2) The action on gelatin which resembles that of the staphylococci.

(3) Its activity in peptonizing milk and coagulated blood serum in which it differs from all the above-named pyogenic cocci.

In virtue of this last property and for the purpose of distinguishing it for the present, we propose the name *Micrococcus zymogenes.*

ALFREDO ANTUNES KANTHACK.

Died at Cambridge, England, on the twenty-first of December, 1898, Alfredo Antunes Kanthack, M. A., M. D., F. R. C. P. (London), Fellow of King's College and Professor of Pathology in the University of Cambridge.

This announcement is a cruel blow to those who have had the good fortune to know and work with this brilliant man. Born in Brazil in 1863, the son of the former British consul at Para, Kanthack received much of his early education in Germany. Studying in England at the University College in Liverpool and at London University, he obtained his B. A. in 1884, his intermediate M. B. in 1885, and B. Sc. in 1886. Pursuing his studies at St. Bartholomew's Hospital, he received in 1887 the double qualification of M. R. C. S. and L. R. C. P. In 1888 he obtained the F. R. C. S. as well as the M. B. and B. S. (London), with honors, receiving also the gold medal for obstetrics. The year 1889 Kanthack spent in work under Virchow in the pathological laboratory at Berlin, but he was compelled in 1890 to leave, in the midst of some important investigations, to serve as obstetrical assistant in St. Bartholomew's Hospital under Dr. Matthews Duncan.

In the summer of 1890 he went to India as one of the commissioners appointed by the Royal College of Physicians, the

Royal College of Surgeons and the Executive Committee of the National Leprosy Fund to inquire into various points with regard to leprosy in India. A large share of the voluminous report of the commission was his work. Returning from India he became the John Lucas Walker student at Cambridge, but in 1892 he went to Liverpool with the intention of practising medicine. Here he held the post of medical tutor and demonstrator of bacteriology at the Royal Infirmary. Later, however, he went to London as director of the pathological laboratory, lecturer on pathology and bacteriology, and curator of the pathological museum at St. Bartholomew's Hospital. In 1896, during the illness of Professor Roy, he was appointed his deputy, and finally in the fall of 1897 he became professor of pathology at the University of Cambridge. In the same year he became an F. R. C. P., and was given the honorary degree of M. A. at Cambridge.

In his school days Kanthack had planned to devote his life to classical studies, and it was a disappointment to him at first to be compelled to turn to what he feared must be a more practical career; but from the beginning his energy and ability brought him enthusiasm and success. In the laboratory at Berlin he earned the admiration of all who knew him, and his early work in Virchow's Archiv on the pathology of the larynx* gained for him the recognition of many others. By no one was he more appreciated than by his great "Master" as he reverently called him, whose attitude toward his pupil was one of genuine affection.

The feeling of his contemporaries cannot be better shown than by quoting in full the cordial letter of Prof. Langerhans, written at the time of his application for the professorship of pathology at Cambridge:

"Herr Dr. med. Alf. A. Kanthack, zur Zeit in Cambridge, hatte vom Sommer 1889 bis August 1890 im Berliner pathologischen Institut einen Arbeitsplatz in demjenigen Arbeitssaal inne, welcher für vorgeschrittene, selbstständige wissenschaftliche Arbeiter bestimmt ist und für welchen ich damals als zweiter Assistent von Rudolf Virchow meinem Chef gegenüber verantwortlich war. In dieser Eigenschaft bin ich damals täglich mit A. A. Kanthack zusammen thätig gewesen und bestätige ich hierdurch, dass sich Alf. A. Kanthack durch sein umfassendes Wissen, eiserne Energie, unermüdlichen Fleiss, durch seine grosse Wahrheitsliebe und strenge Selbstkritik und durch seine feinen, liebenswürdigen und gewinnenden Umgangsformen die Achtung und Liebe aller, die mit ihm in Berührung kamen, gewonnen und dauernd erhalten hat."

Kanthack had published a considerable number of valuable scientific communications, a few of the more important of which were, perhaps, the researches referred to concerning the larynx, his studies upon snake poison,* his various communications with relation to leucocytosis, chemotaxis and immunity,† his studies on mycetoma,‡ his Jackson Prize Essay on the bacillus of tetanus, and his further contributions to the same subject with Dr. Connell,§ and his admirable article upon the general pathology of infection in the first volume of Clifford Allbutt's System of Medicine. He also published in 1894, in association with Dr. Rolleston, a "Manual of Practical Morbid Anatomy, being a handbook for the post-mortem room," and in 1895 with Dr. Drysdale, a "Course of Elementary Practical Bacteriology, including Bacteriological Analysis and Chemistry."

He superintended the observations upon the Tsetse fly disease for the Royal Society, and one of his last publications related to this subject.‖

Much of his work, however, through his modesty and generosity, remained unknown. Only his more intimate friends are aware of the fact that he was the first to succeed in cultivating the parasite of actinomycosis. Compelled in January, 1890, to leave Berlin in the midst of his experiments, he made all possible arrangements for the preservation of his cultures, but on his return, they had, unfortunately, "died out" and another observer had anticipated him with the discovery.

A large share of his energy was given to the help and instruction of others who will bear the warmest testimony to the true worth of their friend and teacher.

His uncompromising honesty, his hatred of anything superficial or incomplete, combined with an active, keen, discriminating mind, and it seemed, an almost unlimited power for work, were a source of admiration to all who knew him. His amazing energy and capability for work were, however, too much even for a fine athletic physique, and his friends had for some years before his death looked with anxiety upon the amount of labor which he crowded into the day.

To the writer Kanthack always seemed the most brilliant of

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*Beiträge zu der Histologie der Stimmbänder mit specieller Berücksichtigung des Vorkommens von Drüsen und Papillen. Arch. f. path. Anat., etc., Berl., 1889, cxvii, 531–544; Studien über die Histologie der Larynxschleimhaut—I. Die Schleimhaut des halbausgetragenen Foetus. Ibid., 1889, cxviii, 137–147; Zur Histologie der Stimmbänder: Erwiderung auf den vorstehenden Artikel des Herrn Prof. B. Fraenkel. Ibid., 376–381; Studien über die Histologie der Larynxschleimhaut. Ibid., 1890, cxix, 326; cxx, 273.

*The Nature of Cobra Poison. Journ. Physiol., Camb., 1892, xiii, 272–299. Report on Snake Venom in its Prophylactic Relations with Poisons of the Same and of Other Sorts. Rep. Med. Off. Local Gov., Bd. (1895–6), Lond., 1897, 235–266.

† Acute Leucocytosis Produced by Bacterial Products. Brit. Med. Journ., Lond., 1892, i, 1301–1303; Immunity, Phagocytosis and Chemotaxis. Brit. Med. Journ., Lond., 1892, ii, 985–989; (with Hardy) On the Characters and Behaviour of the Wandering (migrating) Cells of the Frog, especially in Relation to Micro-organisms. Proc. Roy. Soc. Lond., 1892, lii, 267–273, and Phil. Tr., Lond., 1895, clxxxviii, 279–318; (with Wesbrook) Report on Immunity Against Cholera: An experimental inquiry into the bearing on immunity of intracellular and metabolic bacterial products. Brit. Med. Journ., Lond., 1893, ii, 572–575; (with Hardy) The Morphology and Distribution of the Wandering Cells of Mammalia. Journ. Physiol., Camb., 1894, xvii, 81–119.

‡ Madura Disease (mycetoma) and Actinomycosis. Journ. Path. and Bact., Edinb. and Lond., 1892, i, 140–162.

§ The Flagella of the Tetanus Bacillus and Other Contributions to the Morphology of the Tetanus Bacillus. Journ. Path. and Bact. Edinb. and Lond., 1896–7, iv, 452, and Trans. Path. Soc. Lond. 1896–'97, xlviii, 271–279.

‖ Kanthack, A. A., H. E. Durham and W. F. H. Blandford: On Nagana or Tsetse Fly Disease. Proc. Roy. Soc., Vol. 64.

ontemporaries. His ideals were the highest; and never was in truer to his ideals. An exacting and searching critic of friends, he was a severer critic of himself. This amounted etimes to self-depreciation; it was indeed, on such occas, almost pathetic to note the apparent unconsciousness of own superiority.

And with his high ideals he was ever full of practical sug-tion. He never tired of urging the necessity of a more ieral introduction of accurate and scientific methods into dicine. His last public address* was an earnest appeal for ore systematic and thorough clinical study in hospitals and hools.

His influence which was beginning to be generally felt in his vn country was destined to have a far wider sphere. The ss of such a man is hardly greater to his university and to his iends than to the world at large.

Personally, Kanthack was the simplest and most lovable of ien.

In 1895 he married Lucie, the daughter of F. Henstock, Esq., of Liverpool. W. S. T.

NOTES ON NEW BOOKS.

Operative Gynaecology. By Howard A. Kelly, A. B., M. D.; Professor of Gynaecology and Obstetrics in Johns Hopkins University, Baltimore; Gynaecologist and Obstetrician to Johns Hopkins Hospital, Baltimore. 2 vols., 550 pages each, with 48 plates and 592 original illustrations. (*D. Appleton, New York*, 1898.)

This work is practically a series of clinical lectures, thoroughly and exquisitely illustrated by drawings from cases which have been under the author's care.

Volume No. I contains nineteen lectures upon the following topics:

1. Sepsis, asepsis, and antisepsis in hospitals.
2. Antisepsis and asepsis in private practice.
3. Bacteriology.
4. Topographical anatomy.
5. The gynaecological examination.
6. Gynaecological instruments and dressings.
7. Anaesthesia.
8. General principles involved in plastic operations.
9. Diseases of the external genitals.
10. Rupture of the recto-vaginal septum and relaxed vaginal outlet.
11. Operations on the vagina.
12. Affections of the urethra and bladder.
13. Affections of the ureters.
14. Operations upon the cervix of the uterus, including dilatation and curettage.
15. Prolapse of the uterus.
16. Vaginal hysterectomy.
17. Inversion of the uterus.
18. Vaginal extirpation of the submucous myomata and polypi.
19. The uterus as a retention cyst.

The contents of Volume II are:

20. General principles and complications common to abdominal operations.
21. Care of wound and patient up to recovery.
22. Complications arising after abdominal operations.
23. Tubercular peritonitis.
24. Suspension of the uterus.
25 Conservative operations on the tubes and ovaries.
26. Simple salpingo-oöphorectomy and salpingo-oöphorectomy for adherent tubes and ovaries.
27. Vaginal drainage and enucleation for pyosalpinx, ovarian abscess, tubo-ovarian abscess, and pelvic abscess.
28. Hysterectomy, with extirpation of ovaries and tubes, abdominal hystero-salpingo-oöphorectomy.
29. Ovariotomy.
30. Abdominal hysterectomy for carcinoma and sarcoma of the uterus.
31. Myomectomy—hystero-myomectomy.
32. Operations during pregnancy.
33. Cesarean section.
34. Extra-uterine pregnancy.
35. The radical cure of hernia.
36. Intestinal complications.
37. The more remote results of abdominal operations.
38. On the conduct of autopsies, the making of protocols, and the preservation of tissues for microscopic examination in gynaecological practice.

Those who have been fortunate enough to see Dr. Kelly at home, will, while reading the work, easily imagine themselves in his operating room, listening to a brief history of the case to be operated upon; a review of the anatomy of the parts; a description of the operation to be done; the reasons for selecting this special procedure; the difficulties and dangers to be met, and the best way to overcome them. The style throughout is conversational, clear, concise, clean-cut, and impresses one with the feeling that the writer is presenting a frank statement of his experience in the treatment of the different diseased conditions met with in abdominal surgery.

Few books have been more eagerly looked for; few have so fully realized our expectations. The author in the opening paragraph of his preface says: "My aim in writing this book has been to place in the hands of many friends who have from time to time visited me, and followed my work, a convenient summary of the various gynaecological operations I have found best in my own practice. It is far from my purpose to present a digest of the literature of the subject, or even to describe all the important operations." The claims to originality are mainly connected with the operation for suspension of the uterus, the investigation of vesical and ureteral diseases, and with Kelly's modification of abdominal hysterectomy for fibroids. The chapters on sepsis and antisepsis, bacteriology, the conduct of autopsies, and preservation of tissues for microscopical examination, have been written with the assistance of acknowledged authorities in these several departments, and are deserving of more attention than is commonly given to chapters devoted to these subjects in surgical text-books.

However much we may desire to give special attention to individual chapters, the space at our disposal would preclude this, and we are compelled to speak of the work as a whole, and to present our impressions of it in a few sentences.

At first sight many will be inclined to think that the illustrations are the feature of the work, but those who have had any experience in abdominal surgery and its difficulties, and have read any considerable portion of the work carefully, will feel, that while the illustrations are all that illustrations could be, both from an artistic standpoint and because of their value in assisting the reader to follow the text, the great feature of the work is the careful selection of the best-known treatment for each disease described. Where, as in uterine fibroids, extra-uterine pregnancy, and pelvic abscess, the conditions in the different cases vary, the procedure best suited to those different conditions is indicated and clearly described. Wherever medical treatment is deemed of use, it is care-

* The Science and Art of Medicine. The Mid-sessional Address delivered before the Abernethian Society on July 7, 1898. St. Bartholomew's Hospital Journal, August, 1898.

fully outlined. The old-time "applications," however, find no place in the work. Where no mention is made of medical treatment it is because nothing can be hoped for from this quarter, and no course of treatment is encouraged which is likely to end in disappointment.

Another feature, and a pleasing one, is the spirit of conservatism which everywhere pervades the book. We find, for example, that par-ovarian cysts are now enucleated without sacrifice of the ovary, contrary to the former practice. In ovarian disease, where the tube is not involved, it is allowed to remain, and in uterine fibroids, when consistent with safety, myomectomy, and not hysterectomy is advised. While the work is of great value to all interested in abdominal surgery, representing, as it does, the most advanced thought of the day, it ought to receive special welcome from those practitioners who live at some distance from hospital centres. Such men, if they study the principles of aseptic abdominal surgery as enunciated in the early chapters of the work, will not only be enabled to retain under their own care cases now referred to the city specialist, but will also be able to extend treatment which, in the past, has only been possible in the larger centres, to those who on account of their limited means cannot avail themselves of the services of a specialist.

Dr. Kelly's original work on suspension of the uterus and affections of the bladder and ureters, places the profession under permanent obligation to him. In originating the operation of suspension of the uterus he has added materially to our resources in the treatment of certain uterine displacements (decensus and retro-displacements). With this operation we have had some little experience, having done upwards of seventy cases with a single relapse, and without mortality. Two patients subsequently became pregnant and were delivered at term of living children, without special discomfort or complication ; two others are advanced four months in pregnancy, without development of any abnormal position of the uterus. If we restrict the operation of ventral fixation to those suffering from displacement and who have passed the menopause, and employ suspension in such as are liable to become pregnant, the operation is likely to increase in favor, as a safe and reasonably certain method of securing relief from local discomforts, as well as from disorders referred to the stomach, spine and legs. Certainly in no class of cases have we met with greater gratitude, or seen more marked improvement in general health, than in those selected for this operation.

The easy use of the cystoscope and ureteral catheter requires a little experience and manipulative skill. To those who possess these requisites, Kelly's cystoscope and ureteral catheter will prove invaluable instruments, enabling them to recognize and relieve distressing conditions not generally diagnosed and therefore not corrected by the ordinary practitioner. Those who have mastered the use of these instruments, and this with a little perseverance is easily possible to all, will not long remain in doubt as to their value.

The work is an embodiment of modern ideas clearly and concisely presented in good order, and well represents the most advanced operative gynaecology of the day.

LESSLIE M. SWEETNAM.

BOOKS RECEIVED.

Atlas of Legal Medicine. By Dr. E. von Hofmann. Authorized translation from the German. Edited by F. Peterson, M. D., assisted by A. O. J. Kelley, M. D. 1898. 12mo. (Saunders' Medical Hand-Atlases.) W. B. Saunders, Philadelphia.

Index Catalogue of the Library of the Surgeon-General's Office, United States Army. Authors and Subjects. Second Series, Vol. III. C—Czygan. 1898. 4to. 1100 pages. Government Printing Office, Washington, D. C.

A Pocket Medical Dictionary giving the Pronunciation and Definition of the Principal Words Used in Medicine and the Collateral Sciences, etc. By George M. Gould, A. M., M. D. A new edition entirely rewritten and enlarged, including over 21,000 words. 1898. 16mo. 530 pages. P. Blakiston's Son & Co., Philadelphia.

Twentieth Century Practice. An International Encyclopedia of Modern Medical Science by Leading Authorities of Europe and America. Edited by Thomas L. Stedman, M. D. In Twenty Volumes. Vol. XVII. Infectious Diseases and Malignant New Growths. 1898. 8vo. 715 pages. Wm. Wood & Co., New York.

Archives of Neurology and Psychopathology. Vol. I., Nos. 1-2, 1898. 8vo. 262 pages. State Hospital Press, Utica, N. Y.

Diseases of the Eye. A Handbook of Ophthalmic Practice for Students and Practitioners. By G. E. de Schweinitz, A. M., M. D. Third Edition. 1899. 8vo. 696 pages. W. B. Saunders, Philadelphia.

A Manual of Physiology. With Practical Exercises. By G. N. Stewart, M. A., D. Sc., M. D., Edin., D. P. H., Camb. Third Edition. 1898. 8vo. 848 pages. W. B. Saunders, Philadelphia.

A Text-Book of Mechano-Therapy. (*Massage and Medical Gymnastics.*) Especially Prepared for the Use of Medical Students and Trained Nurses. By A. V. Grafstrom, B. Sc., M. D. 12mo. 1899. 139 pages. W. B. Saunders, Philadelphia.

Saunders' Pocket Medical Formulary. By Wm. M. Powell, M. D. Fifth Edition. 1899. 16mo. 290 pages. W. B. Saunders, Phila.

The Treatment of Disease by Physical Methods. By Thomas Stretch Dowse, M. D., Abd., F. R. C. P., Ed. 1898. 8vo. 412 pages. John Wright & Co., Bristol.

A Text-Book of Obstetrics. By Barton Cooke Hirst, M. D. 1898. 8vo. 846 pages. W. B. Saunders, Philadelphia.

Purity and Truth. Self and Sex Series. What a Young Man Ought to Know. 1897. 16mo. 281 pages. The Vir Publishing Co., Phila.

Translation of Lectures Delivered by Aurelio Bianchi, M. D., Parma. On the Phonendoscope and its Practical Application. With Translation of Special Articles by F. Regnault, M. D. and M. Anastasiades, M. D. Translated by A. G. Baker, A. M., M. D. 1898. 8vo. 77 pages. G. P. Pilling & Son, Philadelphia.

Cleft Palate; Treatment of Simple Fractures by Operation; Diseases of Joints, etc. By W. Arbuthnot Lane, M. S. 1897. 12mo. 278 pages. The Medical Publishing Co., Limited, London.

Transactions of the American Gynecological Society. Vol. XXIII. 1898. 8vo. 491 pages. Wm. J. Dornan, Philadelphia.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains announcements of courses of lectures, programmes of clinical and pathological study, details of hospital and dispensary practice, abstracts of papers read and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

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AN ANALYSIS OF THE CASES OF TABES IN THE JOHNS HOPKINS HOSPITAL AND DISPENSARY FROM ITS OPENING IN MAY, 1889, TO DECEMBER 1, 1898.

By H. M. Thomas, M. D., *Clinical Professor of Nervous Diseases, Johns Hopkins University, Neurologist to the Johns Hopkins Hospital.*

In the records of the Dispensary of the Johns Hopkins Hospital there are one hundred histories which have been classed as tabes. Of these I have excluded eight histories, either because the records are too incomplete, or because the diagnosis seems to have been a mistaken one. Twenty-seven cases have been treated in the wards of the Hospital, but unfortunately for the purposes of this paper, many of them were private patients in whose histories the records are often not complete.

Eight (8) of the patients were treated both in the wards of the Hospital and in the dispensary, and we therefore have for comparison the histories of 111 cases of tabes. That these histories are not all equally good, need not be said, and, indeed, not a few of them leave much to be desired.*

* After having read through some 130 histories, I feel that I might with propriety make some observations upon the taking of histories, which, if followed, would be useful at least to the one who has to tabulate them, but I shall not, only saying as I pass, that it is a subject which deserves more attention than is often given to it.

Race.—White, 106; negroes, 5. Of the 106 white patients 70 were born in this country, 17 were Germans, 6 were Irish, and England, Scotland and France were each represented by 2; 6 patients were simply registered as white.

The small number of negroes is of particular interest, and deserves more detailed attention. We have, as I have just said, seen but five colored patients, in whom the diagnosis of tabes seemed in the least justifiable; that is to say, but 4.5 per cent. of our cases of tabes have any discoverable African blood in their veins, for it is to be remembered that in the eye of the law and of the statistician it takes but very little African blood to make a negro.

In the two years ending November 1, 1898, there were registered in the dispensary 35,796 new cases. Of these 3598 were negroes. This makes the negroes represent a little more than 10 per cent. (10.05 per cent.) of the new cases treated. In the cases of tabes, however, our percentage of negroes is only 4.5, which is less than half what it should be if the negroes were represented in their proper proportion. This difference, although interesting in itself, is hardly great enough to warrant

much attention were it not for other considerations. I think I shall not be accused of exaggeration when I state that the great majority of physicians who are qualified to judge have come to the belief that syphilis is the chief, if not the only, cause of tabes.

We in the South know that syphilis is a very common disease among the negroes, but upon examining the records of the dispensary, I was surprised to discover how common it is. In the two years selected for comparison there were treated in the Genito-Urinary and Skin Departments 228 men who were suffering either from the primary syphilitic sore or the secondary skin eruptions. Sixty-three of these men were negroes, that is 27.63 per cent. of the whole number. When we compare this percentage with that which the negro men represent in the whole number of the men registered in the dispensary, during these years, is quite startling. There were registered 17,888 white males and 1223 colored males, *i. e.* 6.39 per cent. of colored males. Unfortunately there are included in this males of all ages, and so the comparison is not perfectly fair; but I believe the error is not great. We have then, during these two years, the negro males, representing 6.39 per cent. of all the males treated in the dispensary, but of the cases of syphilis seen in men during this time, the negroes make up 27.63 per cent.

If we determine the percentage which the cases of syphilis in white and black men, treated in the Skin and Genito-Urinary Departments during two years, bears to the whole number of males of each color admitted to the dispensary during that time, we find it is for the whites 0.91 per cent. while for the negroes it is 5.15 per cent. From this it would seem that in the men coming to this dispensary, the percentage of early syphilis is more than five and a half times greater in the negro race than it is in the white.

Sex.—Men, 92 white, 5 colored—97; women, 14 white—14. That is, the women represented about 12.6 per cent. of the whole number. In the dispensary the percentage of women suffering from tabes is smaller, being a little more than 9 per cent. (9.17 per cent.), whereas female patients represent a little more than 46 per cent. of all patients in the dispensary. In the cases of tabes treated in the wards of the Hospital, the percentage of women is distinctly larger than in the dispensary, reaching 25 per cent.

It is interesting to note that in the first 50 cases treated in the dispensary there was but one woman, and that she was the 50th case. On the other hand, in the wards, 3 out of the first 5 cases were women. This shows how very unreliable such statistics are unless a very large number of cases is considered.

Five of the patients were seen in the private wards of the Hospital and were from the higher strata of society. This is contrary to the usual statement that tabes affects women of the lower classes far more frequently than those who are more fortunately situated. Moebius, out of 40 cases, found only one belonging to the upper classes.

This relative immunity that women appear to enjoy from tabes cannot be due altogether, I believe, to the fact that fewer women suffer from syphilis than men. That syphilis is more common among men seems to be universally believed, and I have no doubt is true as a general proposition.

In certain classes of society, however, the difference, if it exists at all, cannot be great. As an illustration of this, the records of the Skin Department are instructive. During the two years preceding November, 1898, 130 men and 121 women were treated for the skin manifestations of syphilis, but during this time, more men were admitted to the dispensary in general, as well as to the skin clinics, so that if these figures indicated anything as to the liability of syphilis, it would seem that women are slightly more liable to the disease than men. We have as yet seen no case of tabes in a negro woman,* whereas syphilis is most common in them; 42 of the 121 cases of skin syphilis in women were negresses, *i. e.* 34.87 per cent. The percentage of black females to the whole number of females in the dispensary is 14.23 per cent.

Age of Onset.	No.
25–29	8
30–34	17
35–39	24
40–44	27
45–50	16
50 and over.	15
Total,	107

The time of onset of the disease showed nothing of very great interest. Most of the cases developed between 30 and 50. The youngest case was 25, and the oldest 66. The series includes 15 cases which developed after 50, and this is a larger number than would be expected. It may be doubted whether these senile cases should be included, but I do not see how we can do otherwise when the patients present the symptoms and signs that would have led to the diagnosis of tabes had they occurred at an earlier age.†

The onset of tabes is often very insidious and the early stages may last for many years and it seems probable that some of these patients may have been unconscious or may have forgotten the first symptoms.

Duration of the Disease at the Time of Examination.—Cases, 104. This could be determined with more or less accuracy in 104 cases. Duration 1 year or less, 18 cases; between 1 and three years, 34 cases; between 3 and 5 years,

* Since this analysis was made we have examined a colored woman in the Neurological Dispensary (No. 9525) who is suffering from symptoms that indicate tabes; irregular pains, numbness of the feet, difficulty in walking, loss of knee kicks, objective sensory disturbances on legs. The pupils were normal, and no history of syphilis could be obtained.

† Neurol. No. 2947. A man 70 years old, who gave the history of having had a venereal sore at 25, which was followed by a doubtful secondary skin eruption, came to the dispensary complaining that for the last 4 years he had had difficulty in walking in the dark. He had also had slight shooting pains and his feet felt numb. His pupils were of normal size. They reacted very slightly to light, the left better than the right. Both pupils reacted well during accommodation. His knee jerks were absent, his walk was stamping, the heel being brought down first, and he was unable to stand firmly with eyes closed. There was considerable anæsthesia of his legs.

17 cases; between 5 and 10 years, 24 cases; between 10 and 20 years, 10 cases; 30 years, 1 case.

Most of the cases (69) were seen during the first 5 years of the disease, but in 11 cases it had lasted 10 years or more, once even reaching 30 years.

Etiology.—Believing as we do that syphilis is the cause of the vast majority of cases of tabes, we have practically confined our attention to this factor.

Only men have been considered in the following table, and there are definite notes in 95 of the 97 cases.

Exposure to venereal contagion denied... 3			
Exposure admitted but infection denied.. 7			
Infection denied (exposure?) 7			
Venereal infection denied.....	17	17.89	per cent.
Gonorrhœa alone.. 18			
Venereal sore denied.....	35	36.84	"
Gonorrhœa with chancre—indefinite. ...15			
Gonorrhœa with syphilis 20			
Gonorrhœa*	53	55.78	"
Chancre, syphilis.....38			
Syphilis with no history of chancre..... 2			
Certain syphilis.....	40	42.1	"
Chancre indefinite.....20			
Possible syphilis.....	60	63.1	"

By certain syphilis is meant the definite history of a chancre which was believed to be syphilitic and was treated as such, or the history of a chancre which was followed by secondary manifestations, and in two instances, where skin eruptions were recognized as syphilitic, although there was no history of the primary sore. All other venereal sores have been tabulated as indefinite chancres.

In taking the histories, the supposition has been that in all cases of tabes syphilis has preceded, and the burden of proof has been with the patient who denied its presence.

The results are: Certain syphilis, 42.1 per cent.; possible or probable syphilis, 63.1 per cent. These figures fall below those obtained by many of the later observers, but it is not due to lack of zeal.

Some time ago I analyzed the sexual histories of 1238 men who came to the Neurological Dispensary suffering from all sorts of troubles; in them I found certain syphilis in 10.9 per cent., and possible or probable syphilis in 21.4 per cent.

These percentages are much smaller than those found in tabes and the inference that syphilis bears an important relation to the development of tabes is plain, but I must resist the temptation of entering fully into the discussion of syphilis as the cause of tabes. It may not be, however, out of order to sum up what the cases studied here seem to show:

1. In a large proportion of cases of tabes, a history of syphilis can be obtained.

2. In a certain and not inconsiderable number of cases there is no history of a venereal sore or other syphilitic manifestations.

3. In negroes, tabes is relatively uncommon, whereas syphilis is much more common in them than in the white population.

4. The partial immunity of women is greater than can be satisfactorily accounted for by the relative infrequency of syphilis among them.

I do not take these conclusions as indicating that syphilis is not the most important cause of tabes; on the contrary, they seem to me to speak in favor of this belief. The fact that we were unable to elicit the history of syphilis in 36 per cent. of our cases does not of course prove that syphilis was not present in a large proportion of these cases.

Although tabes does not seem to be common in the negro, when it does occur, it has usually been preceded by syphilis. In four of our five cases there was the history of a venereal sore, and the same has been shown in the cases of tabes in women.*

That syphilis is not the only factor in this causation of tabes does seem to be shown. What the factors are that make white men so much more liable than black women to the development of tabes, I am sure I do not know; but of this I feel reasonably certain—that it is not due simply to the difference of primary syphilis among them. To say that it is due to a racial and sexual difference in the power of resistance of the nervous system, does little more than restate the facts.

Virchow† has lately raised his voice against the methods of study which have led to the all but universal belief that tabes is always directly dependent upon preceding syphilis.

The time between the syphilitic infection and the first symptoms of tabes varies a good deal. This point was determined in 47 cases.

Tabes developed after the venereal sore in 47 cases. In the first 5 years, 6 times; in the second 5 years, 10 times; in the third 5 years, 13 times; in the fourth 5 years, 10 times; in the fifth 5 years, 4 times; after 25 years, 4 times.

The shortest interval was 2 years, and the longest intervals were 26, 27, 30 and 42. It occurred about equally in the second, third and fourth five years.

As to the other causes of tabes, our histories show nothing important.

Initial Symptoms.—Either alone or associated, the following symptoms occurred as initial symptoms: Pain, 57 times; ataxia, 24 times; numbness, extremities, 6 times; eye symptoms, 20 times; nausea and vomiting (gastric crises), 4 times; paralysis of bladder, 5 times; loss of sexual power, 1 time; paralytic attacks, 2 times; mental symptoms, 1 time; neurasthenia, 1 time.

Pain.—Pain was the first symptom in the majority of cases, occurring first or very early in the disease 57 times. It was unassociated 41 times and accompanied by other symptoms 16 times.

Ataxia.—Difficulty in walking and ataxia were the first symptoms 15 times, and were associated with other symptoms 9 other times.

Eye symptoms.—Double vision was the initial symptom 6 times. Dimness of vision occurred first alone 4 times. Double vision and dimness of vision were associated once, and double

* Note.—In some of the early cases the history in regard to gonorrhœa was not particularly noted and for this reason the number given is probably too small.

* Kron. Deut. Zeitschr. f. Nervenheilk., XII—1898, p. 303. "Ueber tabes dorsalis beim Weiblichen Geschlecht."

† Centralb. f. Nervenheilkunde in Psychiat., Nr. 105, 1898, p. 625.

vision with other symptoms 7 times. Ptosis was the first symptom, associated with pain twice.

Numbness of extremities occurred alone 4 times, with pain twice.

Paralysis of the bladder occurred alone 4 times, with pain twice.

Subjective Sensory Symptoms—*Pain.*—In 71 cases pain was a prominent symptom. This was usually described as the characteristic lightning or shooting pain. In most cases it was severe, but in some it was mild. The pains were usually localized in the legs, but in three cases they were confined to the body, and in two to the arms, and in six others they were more or less general.

Girdle sense or pain, 27.—This symptom was noted as being present in 27 cases. Sense of numbness in the extremities, 45.

Numbness of the feet was complained of 30 times, the patients often describing a feeling as if the floor were not solid or as if they were walking on some soft substance. There was numbness in both the hands and feet 12 times, and in the hands alone 3 times.

Crisis.—Gastric crises, 9. There were nine patients who gave the history of having had gastric crises. In two of the cases the nausea and vomiting were unaccompanied by pain. In one of the cases very typical gastric crisis and Argyll-Robertson pupils were the only symptoms of tabes.

Laryngeal crises, 2. Two of our cases were subject to spasmodic cough; one of them was a typical case of tabes, but in the other the diagnosis was doubtful.

Rectal crisis, 1. One patient complained that early in his disease he had been subject to intense pain that began in the penis and ran to the rectum.*

Eye symptoms—Optic atrophy, 11.—Optic atrophy occurred in 11, possibly 12 cases. The twelfth case was one in which one optic nerve looked as if atrophy had begun. In the other cases it was double.

Eye muscle paralysis, 33.—Transient double vision was noted as having occurred in 20 cases, and in 13 other cases there was a noticeable weakness of one or more of the external muscles of the eyeballs. In one of these cases there was complete external ophthalmoplegia.

Ptosis was present in 7 cases, and in 1 there was nystagmus.

Pupils—Size.—The pupils were unequal in 30 cases. The left was larger than the right 18 times while the right was the larger 8 times. In four instances the history did not specify which was the larger.

There was contraction of the pupils in ten cases and they were noted as dilated twice.

Pupillary reflexes.— Argyll-Robertson pupils, 70. Both pupils immovable to light, reacted well during accommodation, 59. In one eye, 3. Reacted slightly to light, well to accommodation, 8.

The pupillary reflexes were said to be absent 8 times, and weak 3 times. They were found to be normal 21 times.

Ataxia.—Ataxia was present 91 times: in the legs alone, 78 times; in the arms alone, 2 times; in both arms and legs, 11 times. There was no ataxia 8 times.*

Romberg's symptom, 82.—Present 82 times, marked 59 times, slight 23 times, absent 7 times, not noted 22 times.

Ataxia with optic nerve atrophy.—In the cases which showed atrophy of the optic nerve, ataxia was marked in 2 cases. It was slight in 8 cases and was absent in 1. In two of the cases Romberg's symptom was marked in spite of the patients being blind. It was very slightly marked in 4 cases, and was absent in 4 and not noted in 1.

Deep reflexes.—The knee jerks were absent 87 times; weak 6 times; normal 4 times; not noted 14 times.

Bladder.—The condition of the bladder was noted in 83 cases: Weakness, 35 times; paralyzed, 19 times; normal, 29 times.

Sexual power.—The sexual power was inquired into in 75 cases: Power and desire lost, 38 cases (marked increase before the loss in 3 cases); power and desire weakened, 24 cases; power lost, desire retained, 1; power and desire increased 1; normal, 10; sexual power present, intercourse without sensation, 1 case.

Objective sensory disturbances.—There are definite notes in this respect in 90 cases: Objective sensory disturbances were present in 78 cases; absent in 12 cases.

These were more often in the legs (40 times), but were also demonstrated in the arms and about the chest.

Definite areas of anæsthesia were marked out about the chest in several cases, but this was looked for and not found in more cases. The number of examinations, however, was not sufficient to make the definite proportions of any great value.

Muscular sense.—There were definite notes in 44 cases. In these it was disturbed 38 times, normal 6 times.

Trophic disturbances— Charcot's joints (Arthropathies).—These occur in a typical manner in 5 cases. There was suspicious enlargement of the joint in 3 cases.† In the 5 cases it occurred 3 times in the knee joints, 1 in the shoulder, and 1 in the elbow.

Perforating ulcer.—This occurred 5 times.

Mental Symptoms.—There were mental symptoms present in seven cases, and in one case there was a history of a previous attack of acute insanity, and in one epilepsy had been present from the 14th year up to the time of the onset of tabes, at 44. Since then there had been no fits.

In the 7 cases showing mental symptoms general paresis was suggested. In two of the cases this disease developed while the patients were under observation.

* Since this list was completed I have seen another case of tabes that complained of the same symptom.

* In eight (8) of the cases the ataxia developed quickly. At times this followed an accident, but at other times there was no cause that could be determined. In most, if not all, of the cases, symptoms of tabes had been present for some time before the acute development of the ataxia.

† In one of these patients, who, since this was written, has returned to the dispensary after an absence of two years, and who had, at the time of his first examination, in 1897, a suspicious swelling of the last phalangeal joint of the left index finger, there has developed an undoubted tabetic arthropathy of the right thumb. This patient also had a healed perforating ulcer.

ON TYPHOID SEPTICÆMIA, WITH THE REPORT OF TWO CASES, ONE OF WHICH WAS A TYPHOID INFECTION WITHOUT INTESTINAL LESIONS.

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Our knowledge of the various forms of typhoid infections has rapidly increased within the past few years, and more particularly that regarding the character of those atypical and more rare forms, the chief interest of which lies in the singularity of localization of the typhoid bacillus. The value of the contributions of recent years is largely the outcome of improved bacteriological technique and closer and more accurate study of the natural history, cultural behavior and experimental manifestations of the bacillus typhosus and the bacillus coli communis. Investigators have appreciated more and more the necessity of exact methods of differentiation between bacterial forms, and especially between more or less closely allied species, such as the bacillus of typhoid fever and the colon bacillus.

The absence of precise methods of differentiation between these two micro-organisms by the earlier workers in this field has, of necessity, thrown much discredit upon the conclusions and results of otherwise much good and brilliant work. The belief of the passage into, and existence of, the typhoid bacillus in the blood of the general circulation is by no means a new one, as shown by the writings of some of the early writers who worked upon typhoid fever. Rütimeyer, Almquist, Meisels, Neuhaus, and others, claimed to have cultivated the bacillus from the general blood and that of the rose-spots during life, but their work, through the latter researches of Janowski, Stagnitta, Grawitz, Fraenkel and Simmonds, and Sittman has not received acceptance. According to some observers the typhoid bacillus in almost every case at some time of the disease escapes into the general circulation from the more common foci of infection.

This view has received some support from the investigations of late years, demonstrating the great multiplicity of localization of Eberth's bacillus in the human economy: lesions of the bones, pulmonary implications, uterine infection, abscesses of various nature, etc., in all of which the organism has been found in pure culture. Wright and Semple[1] and Sanarelli[2] and other observers regard typhoid fever as primarily a blood infection, the two former writers basing their contention largely upon the fact that in the urine of almost every case suffering from typhoid fever they were able to find the specific organism. Recent researches, however, show more and more conclusively that the typhoid bacillus is not, commonly, to be found in the blood of the general circulation. The explanation of this apparent discrepancy between the results of Sanarelli, and Wright and Semple and other observers, who from their investigations have shown that the bacillus is only infrequently found in the general circulation, is to be found probably in the suggestive experiments of Wyssokowitsch[3] and the observations of Welch and Nuttal[4]. The first experimenter in some very interesting experiments upon rabbits was able to show that the organs in which typhoid bacilli are commonly found play a very important rôle in the removal of introduced bacteria from the blood. After injecting pure cultures of the typhoid bacillus into the blood the animals were sacrificed at the end of eighteen hours, and bacteriological examination invariably failed to show bacilli in the blood of the general circulation, but always showed them in great numbers in the spleen. Welch and Nuttal in 1891, on the other hand, demonstrated the bactericidal properties of human blood serum for the typhoid bacillus, an observation since confirmed by a host of investigators.

Instances of typhoid septicæmia diagnosticated during life by isolating the bacilli from the blood are very scanty in number. Bozzolo,[5] Guarnieri,[6] and Silvestrini[7] have reported cases of this nature; Wiltschour[8] in the examinations of 35 cases found it once; Ettlinger[9] similarly succeeded in cultivating it from the blood during life, but a second culture in the same case from the vein of the forearm, the day before the patient's death, gave a doubtful result. Thiemich[10] found it once in the blood taken during life from a vein of the forearm, and Stern[11] was likewise successful in two instances. P. Teissier[12] isolated the typhoid bacillus from the blood of a young man in the 15th day of his disease; Kühnau[13] grew the organism from the blood of a pregnant woman during life in which the subsequent post-mortem findings confirmed the existence of a typhoid septicæmia; more recently this writer[14] has published the reports of nine additional instances in which he found typhoid bacilli in the blood out of 41 cases of typhoid fever submitted to bacteriological examinations. E. Bates Block[15] has reported a very conclusive example of this kind in which the typhoid bacillus was discovered in the blood during life on two different occasions, at an interval of four days. This case presents several interesting features, among others being the fact that a culture taken on the day before the patient's death contained the bacillus typhosus, whilst the bacteriological examination, post mortem, demonstrated its presence only in the spleen, liver, placenta, and kidneys, and the bacillus pyocyaneus in the heart's blood. In the recent Medical and Surgical Reports of the Presbyterian Hospital,[16] Walter R. James and George A. Tuttle report three cases in which they succeeded in isolating the bacilli from the blood during life.

The diagnosis on the autopsy table of general invasion by the bacillus typhosus is far less rare than its recognition during life, but it must not be supposed that as a post-mortem finding it is a frequent occurrence. The very early reports of this kind will not be considered in this paper, since their study was carried on at a time when the differences between the typhoid bacillus and the colon group were less appreciated than now. Karlinski,[17] Vincent,[18] Klein,[19] Banti,[20] Wright and Stokes,[21] Flexner,[22] Carter,[23] Chiari and Kraus,[24] and finally Blumer[25] have contributed a fair number of instances in adults that showed the organism in the blood after death. Typhoid septicæmia is an occurrence of comparatively greater frequency in the fœtus born of a mother suffering from typhoid infection. The passage of the organism from mother to fœtus has repeatedly received demonstration in the observations of

Frascani[26], Janiszewski[27], Freund and Levy[28], Dürck[29], Etienne[30], Marfan[31] and probably earlier observers.

The question of the bacterial associations in this class of infections is an exceedingly interesting one, and especially the influence of secondary infections in modifying the relation of the patient to the typhoid bacillus. Vincent[32] in 1891 called attention to the importance of the streptococcus in typhoidal infections. This observer found in cases of typhoid fever brought to autopsy the streptococcus and typhoid bacillus associated in six out of thirty-one cases. The investigations of Flexner[33] similarly demonstrated the frequency with which the streptococcus is found as a complicating factor in this disease; other observations of the same nature were made by Wright and Stokes[34], Netter[35], E. Fraenkel[36], Karlinski[37], Carter[38], and others.

The recently published case by Blumer[39] deserves special mention, not only as an instance of typhoid and streptococcus septicæmia, but also as a rare example of combined typhoid and streptococcus puerperal infection. The case was that of a married woman, 34 years of age, who was confined by a midwife. On the sixth day of the puerperium the patient, shortly after a hearty meal, was taken with dyspnœa and incoherency of speech. She rapidly became delirious and semi-comatose. The temperature was 100.8 F. The uterus was apparently normal. Patient died two days after the onset of her trouble. The post-mortem examination showed the existence of typhoid fever: swelling and ulceration of Peyer's patches in the lower end of the ileum, acute splcen tumor and enlargement of mesenteric glands. The cultures from the heart's blood, liver, spleen, and uterine cavity, contained the streptococcus pyogenes and the bacillus of typhoid fever.

For the abstracts from the histories of the two following cases I am indebted to Drs. Henry Hun and Joseph D. Craig, of Albany, New York:

Case I.—Miss A., 20 years of age, came under observation October 19, 1897, complaining of gastric disturbances and fever.

The past history is unimportant, except that three years before she had an attack of grippe, which was accompanied by very irregular and alarming heart action. On the 16th day of October, 1897, the patient was taken ill with nausea, and was actively sick at her stomach. The following day she still felt ill and a physician, who was called in, found a temperature of 102° F., together with a very decided degree of prostration. The patient brought under observation at this time did not show any tenderness or gurgling in the right iliac fossa and there had been no diarrhœa. From this time there was fever varying from 102° F. to 106.6° F.—the temperature at the time of her death. The spleen and liver became enlarged, later delirium supervened, vomiting persisted and cardiac weakness became prominent; no diarrhœa at any time. Patient died October 25, 1897.

The autopsy was made on October 26th, 15½ hours after death.

The following notes are abstracted from the autopsy protocol:

Exterior.—Body of a slender-built, moderately well-nourished girl. Rigor mortis well marked all over. Post-mortem lividity in the dependent parts. Pupils mid-wide and equal. Mucous membranes slightly cyanotic. Surfaces of body generally pale, subcutaneous fat moderate in amount. Abdominal muscles of a homogeneous red-brown color. Peritoneal cavity dry, parietal layer smooth; visceral layer shows numerous areas over which there is congestion apparently corresponding to Peyer's patches. Omentum delicate, free from adhesions, completely covering the intestines. Appendix about 9 cm. long, has a distinct mesentery to within 1 cm. of its tip; passes downward and inward across pelvic brim. The liver is visible two fingers' breadth below the costal margin in the mammary line. Spleen not visible. Both pleural cavities were dry; both lungs presented about the same appearance; the upper lobes were slightly congested; the lower and middle lobes on the right side and the lower lobe on the left were much congested, and on pressure a large quantity of dark blood could be expressed. A small quantity of mucus could be expressed from the medium-sized bronchi. Bronchial mucous membrane irregularly congested.

Heart.—Pericardium contains no excess of fluid. Pericardium is smooth. There are a few pin-point sub-pericardial hemorrhages. Heart contains fluid blood. The endocardium on the right side is smooth, the muscle shining through it has a somewhat mottled appearance in places. The tricuspid and pulmonary semilunar valves are normal. The length of the right ventricle is 6 cm.; the average thickness of the wall 4 mm. The pulmonary artery has a circumference of 5 cm. The endocardium of the left side of the heart is, in places, slightly thickened over the auricle. The ventricle is normal. Aortic and mitral valves are normal. Heart muscle is rather flabby and on section has a very cloudy, grayish-brown color, in places somewhat mottled in appearance. In both coronary arteries, which are patent, are small elevated areas of fatty atheroma. Spleen is much enlarged, measuring 17 x 20 x 5 cm. The capsule is smooth, tense; consistency of organ much softer than normal. On section the organ is of a chocolate-red color. The pulp is considerably increased in amount. The Malpighian bodies are plainly visible as pin-point, gray, circular areas. Liver is considerably increased in size, measures 23x19x6½ cm. There seem to be a number of pinhead-sized hemorrhages beneath the capsule; consistency much softer than normal. On section the organ has the typical boiled appearance; the lobules are indistinct, the peripheries being quite yellow where they can be made out. Scattered throughout the organ is a number of pinhead-sized blood-red areas, apparently hemorrhages.

The adrenal glands appear normal.

Kidneys of about the same size, averaging 13 x 4½ x 3 cm. fibrous capsule normal and strips off easily; surface smooth; surface veins little dilated. On section cortex is swollen; cortex markings are somewhat indistinct; the glomeruli barely visible; the medulla congested. Pelvis appears normal.

Stomach and pancreas and female generative organs not examined.

Intestines.—Duodenum slightly bile-stained. Mucous membrane slightly congested; jejunum shows similar changes, but with apparently no ulcerations. In the ileum, beginning 80 cm. above the iliocæcal valve, are a series of lesions affecting the solitary follicles and Peyer's patches. They are least marked in the upper portion of the ileum, where they consist in a great swelling of the lymphatic apparatus. The solitary follicles

measure as much as one-half cm. in diameter. The most recent swollen patches are considerably elevated above the surface. They have a mottled appearance, the predominating color being pink, and the mottling being due to yellowish areas, presumably of necrosis, as in one or two places the surface has been broken and ulcers formed. In the lower portion of the ileum the swelling is much more extensive and the necrosis much more marked. The solitary follicles are often the size of a large pea, their inner surface being capped with an ulcerated area on which a yellow necrotic material is situated. The swollen Peyer's patches in the lower portion of the ileum show, scattered over their surface, numerous ulcerated areas, capped with this same yellowish necrotic material, varying in diameter from 4 mm. to considerably over a cm. The edges of all these ulcerated areas are, in places, distinctly hemorrhagic and, as a rule, the blood-vessels of the intestinal wall can be seen radiating from the edges of the lymphatic apparatus, filled with blood. The lymphatic apparatus of appendix is markedly swollen, but no ulcerations are present. The upper portion of the colon is thickly dotted with swollen solitary follicles. These have an average diameter of about 7 mm., are considerably raised above the surface of the intestine, and show on their inner surface ulcerated areas capped by yellowish necrotic material similar to those seen in the small intestine. They differ from these latter from the fact that their bases are, as a rule, distinctly hemorrhagic, each nodule being surrounded by a distinct zone of submucous hemorrhage. The lower part of the colon is almost entirely free from such areas, but contains a number of discrete or confluent pin-head areas of hemorrhages.

Mesenteric Glands.—Particularly those behind lower portion of ileum are extremely swollen. They are soft in consistency and on section have a mottled appearance, the predominating color being a bright pink, the mottling being due to pin-point gray areas, which are scattered through them, perhaps the swollen follicular portions of the glands.

Anatomical Diagnosis.—Typhoid fever (beginning of second week), with typhoid septicæmia. Swelling of Peyer's patches and the solitary follicles with superficial necrosis and ulceration. Marked involvement of the solitary follicles in the upper portion of the colon. Great swelling of the mesenteric glands. Acute spleen tumor. Cloudy swelling of the heart muscle, liver and kidneys.

The microscopic examination of the heart, lungs, and kidneys adds particularly nothing to the macroscopic observations, except that the heart muscle showed the evidences of a moderate degree of fragmentatio myocardii. The following are the notes from the protocol regarding the microscopic appearances of the liver, spleen, mesenteric glands, and intestines:

Liver.—Capsule is everywhere normal in appearance. The connective tissue is not increased in amount. Liver cells are greatly swollen and extremely granular. Scattered throughout the liver substance are numerous, almost circular areas, presenting varying appearances, according to the stage of development. In some instances the areas show merely an extensive necrosis of the liver cells, many of them in such areas having lost their nuclei, this loss of nuclei giving rise to a light colored patch in the liver substance. Many of the other areas show, besides this necrosis, an infiltration with cells of varying characters. In some of them the necrotic area is infiltrated, for the most part, with small round cells of the lymphoid type. In others, large numbers of irregularly shaped epithelioid cells are present. No giant cells can be made out. The nodules resemble very markedly, in some instances, miliary tubercles, but there is not present a definite arrangement of the two varieties of cell, such as exists in tubercle; but, on the other hand, the two forms are evenly intermingled in the nodules. These nodules apparently bear no definite relation to any particular anatomical structure of the liver in most instances, although at least in one instance the necrotic area lies exactly around the central vein of the lobule. Besides areas of necrosis, there are found scattered through the organ a number of blue-staining areas, usually of much less extent than those occupied by the nodules. These areas have a granular appearance under the low power and which is more marked under the high power. It can be seen, at the edges particularly, that they are made up of individual rod-like structures resembling the typhoid bacilli. The blood-vessels of the liver show no particular change; nor do the bile-vessels.

Spleen.—Capsule not thickened. Trabecular substance is normal in amount. The amount of blood present in the pulp is tremendously increased over the normal. Furthermore, it can be made out with the high power that in a great many instances the red-blood corpuscles are contained in large cells. Scattered throughout the organ are a number of almost circular areas, in which it can be seen with the high power that considerable necrosis exists, as is shown by lack of nuclei and many of the spleen cells, and by the presence of nuclear fragments. These areas, as in the liver, are often infiltrated with lymphoid and epithelioid cells. There are also present in the spleen numerous blue-staining granular collections of bacteria similar to those seen in the liver. In some instances these collections of bacteria are in definite relation with necrotic areas, but this could very rarely be made out in the liver.

Mesenteric glands.—The amount of normal gland structure is very small. Almost the entire gland appears to be in a necrosed condition. In some areas the necrotic foci contain very large quantities of fragmented and destroyed nuclei. In other places very few of these are present. Among the necrotic areas are to be found, as in the liver and spleen, numerous epithelioid and lymphoid cells, some of these latter doubtless being cells which normally belong to the lymphoid glands. The areas of necrosis may possibly have been focal in origin, but in the section under observation they are so extensive that one coalesces with the other all over the gland. There are apparently no clumps of bacteria in this section under observation.

Intestines.—The lesions of the intestine vary. In all cases the superficial layer of the intestine seems to be necrotic to a certain extent, but this at any rate is doubtless due partly to post-mortem change. In the earliest stage of the disease to be made out in these sections, the lymphoid apparatus is tremendously swollen, the cells present in the swollen area no longer being apparently lymphoid in character, but many epithelioid cells are also present. All through the swollen area there are evidences of necrosis in the form of numerous nuclear fragments. In the earlier stages the muscular coat of the intestine

does not appear to be affected. The section which shows a more advanced stage of the disease shows that the progression consists mostly in the extension of the necrotic processes. In some instances the whole involved area is entirely necrotic, almost to the depth of the muscular coat, and there may be present beneath this necrotic material and between it and the muscular coat fibrin, in whose meshes are entangled polynuclear leucocytes and epithelioid cells. In this stage the muscular coat itself usually shows the presence of a few polynuclears and a large number of small round cells or epithelioid cells. Elsewhere in the swollen areas the necrosis is extensive, as in the mesenteric lymph glands. There is hardly an area in the section which has escaped it. In the later specimens the amount of cellular infiltration in the muscular coat is often very large, the muscle fibre being pushed widely apart by it, and in some places being distinctly necrotic over large areas. The infiltrating cells, under these circumstances, seem to be mainly small, round and epithelioid cells with an occasional polynuclear. Blue-staining collections of bacteria are seen in very large numbers in the deeper part of the necrotic areas in some of the sections.

Bacteriologic Report.—Coverslips from the mesenteric glands, spleen and bone marrow all show the presence of medium-sized, short, thick bacilli frequently occurring in clumps. Cultures were taken upon slant agar-agar from the heart's blood, spleen, lung, liver, mesenteric glands, kidney, and bone marrow.

The culture from the heart's blood, after 24 hours' incubation, contained four discrete pinhead-sized, gray-white, slightly elevated colonies. The morphologic appearances showed the presence of a bacillus of moderate length and thickness, apparently a pure growth. Culturally the organism behaved as follows:

Litmus milk.—No acidification or coagulation of the milk after six days' incubation in the thermostat at 37½° C.

Potato.—A moist, just perceptible growth along the line of inoculation.

Bouillon.—Diffuse cloudiness of the nutrient medium. Hanging drop preparations from young cultures show active motility.

Gelatin stab.—Whitish growth along the line of inoculation; no liquefaction of the gelatin.

Dunham.—Diffuse cloudiness of the medium. No indol reaction. No gas formation in saccharose, glucose or lactose media.

Agar slant.—Moderate, moist, whitish elevated growth. This organism, with the serum of an undoubted case of typhoid fever, showed a very positive Widal reaction in dilutions, varying from 1 to 30 to 1 and 50.

Diagnosis.—Bacillus typhosus.

The cultures from the spleen, liver, mesenteric glands and bone marrow similarly contained a pure growth of a bacillus, morphologically and culturally, like the organism isolated from the heart's blood. The typhoid bacillus was also isolated from the kidney associated with the bacillus coli communis. From the lung the colon bacillus was isolated in association with the staphylococcus pyogenes albus.

Case II.—James R., aged 36, admitted into the Albany Hospital, August 8, 1898, suffering from severe headache and pains in the arms and legs. The family history showed nothing of importance, and until the present sickness patient had always been quite well. Four days before admission he was taken ill with violent headache, fever, pains in limbs, and a slight chill. The following morning he went to his work, but felt so much worse that he went home and retired to his bed. The day before entering the Hospital he suffered from a nose-bleed, and had another on his way to the Hospital.

The physical examination shortly after admission was quite negative, but the temperature was 102.2° F. Later on in the disease the liver became slightly, and the spleen very much, augmented in size. The bowels remained constipated from the beginning of the disease, and at no time did the patient complain of abdominal tenderness at any point. There was some vomiting on several occasions, but at no time was the gastric derangement very severe. Toward the end delirium came on. The temperature throughout the disease varied between 99.8° F. and 103°, until the day before his death when the temperature reached 105.2° F. Death August 25th, 1898.

The autopsy notes are as follows:

Body 175 cm. long, moderately well built, considerably emaciated. Rigor mortis in both extremities. Pupils wide and equal; mucous membrane pale; post-mortem lividity of dependent parts. Abdomen tense and very distended, apparently with gas. Walls discolored; patches of greenish blue. Subcutaneous fat nearly absent. Muscles of thorax and abdomen pale and poorly developed.

Peritoneum.—Both layers smooth, glossy and free from injection. Omentum free from adhesions and contains a little fat; omental glands not enlarged. Intestines very distended with gas, particularly small intestines. Left lobe of liver visible below costal margin 5 cm. Stomach not apparent. Peritoneal cavity contains a small quantity of dark-colored, turbid fluid. Appendix measures 13.5 cm. in diameter, normal in appearance and free from adhesions; mesentery present throughout its entire length. Diaphragm fifth space on right side; sixth rib on left. Costal cartilages not ossified. Retro-sternal glands not enlarged. Both pleural cavities free from any excess of fluid.

Pericardium.—Both layers smooth; cavity contains no excess of fluid.

Heart.—Contains red and chicken-fat post-mortem clots, and is distended with fluid blood; normal in size. The endocardium of the right heart shows post-mortem discolorations. Tricuspid valve normal; also pulmonary and semilunar valves. The left heart shows areas of fatty atheroma in auricle; ventricle normal. Mitral leaflets very thick along their free edges. Aortic valves normal. Aorta just above valve shows areas of fatty atheroma. Coronary arteries patent; walls show large confluent patches of fatty atheroma. Heart muscle somewhat soft; on section, of a dark reddish-brown color (brown atrophy).

Left lung.—Bound down by old firm adhesions at the base and posteriorly. The pleura elsewhere is smooth. Lung crepitant; less so in normal than lower lobe. On section, the upper lobe is slightly congested; lower lobe markedly so and

contains quantity of blood-stained serum, which readily escapes. Bronchial mucous membrane congested and covered by a moderate amount of mucus. One portion of the upper lobe contains a pea-sized, firm calcareous mass embedded in the lung substance proper.

Right lung.—Bound down by old firm adhesions laterally and posteriorly. Lobes very much increased in consistency, but still crepitant. On section, the three lobes generally present a similar appearance, and contain a large quantity of blood-stained serum, especially the lower lobe, from which it runs off in abundance. The three lobes are markedly congested. Bronchi and blood-vessels similar to other side. In several places are a number of nodules very firm, sharp, and circumscribed, varying from a small shot to large pea in size. On section, these nodules are calcareous.

Spleen.—Free from adhesions. The organ is very large, measuring 16x6x10 cm. Capsule not wrinkled, and smooth. Consistency much decreased. Trabeculæ not increased. Spleen pulp very much augmented. Malpighian bodies also very greatly augmented in size.

Liver.—Bound to the diaphragm and to the abdominal wall by adhesions. The organ is very much enlarged, measuring 26x20x8 cm. The capsule smooth. Consistency softer than normal. On section the organ is pale and cloudy (cloudy swelling).

Gall-bladder. — Distended with greenish-colored bile. Mucous membrane smooth and normal looking.

Left kidney.—Fatty capsule scanty. Fibrous capsule strips off fairly easily, occasionally tearing bits of kidney substance. The organ is somewhat enlarged. The surface is smooth; veins somewhat prominent. On section the cortex is practically normal in amount; markings quite prominent; glomeruli very distinct and congested. Medulla normal. Pelvis normal.

Pancreas, adrenals and left ureter are normal.

Mesenteric glands not enlarged, or only very slightly so.

Aorta shows occasional patches of fatty atheroma.

Retro-peritoneal glands.—Enlarged, but not markedly so.

The right adrenal gland occupies its normal anatomical position in relation to the surrounding viscera, but below it the kidney is absent. In its place is a small, somewhat firm, mass of tissue 5 cm. long and 2 cm. in thickness, and which, on section, presents a very peculiar appearance, in no manner suggestive of renal tissue. The ureter of this side leads to this mass.

Bladder.—Contains a small quantity of light, turbid urine. The walls are not increased in thickness and the bladder is of normal size.

Intestines.—The small intestines show no injection of the mucous membrane nor are the solitary follicles swollen. In the small intestine Peyer's patches show no evidence of being swollen or of other implication. No evidence of ulceration or cicatrization. The mucous membrane of large intestine is quite normal in appearance.

Anatomical Diagnosis.—Marked œdema and congestion of both lungs; chronic adhesive pleuritis and healed (calcareous) tuberculosis of both lungs. Brown atrophy of heart. Acute splecn tumor; cloudy swelling of liver and kidney; congenital absence of right kidney; slight swelling of mesenteric glands; fatty atheroma of aorta; coronary artery disease.

The microscopic examination of the heart shows some fragmentatio myocardii in addition to the macroscopic findings; the lungs and kidneys microscopically show nothing very striking.

The following are some notes abstracted from the records of the microscopic examinations of the liver, splecn, and mesenteric glands:

Liver.—Capsule is normal in thickness. Connective tissue of the organ does not appear to be increased. The liver cells are swollen and rather indistinct. The nuclei are apparently, as a rule, well preserved. Scattered throughout the section in large numbers are circumscribed areas of focal change. In places as many as three of these can be seen under a low power. The appearance exhibited by these areas varies in different parts of the section. In some of them the process seems to be almost entirely necrotic in character, the liver cells in the area having lost their nuclei and taking rather an intense stain with the eosin. In these areas can be seen a few polynuclears and a number of small, round cells and cells of an epithelioid type. In other portions of the section the areas are extremely cellular and have the typical appearance of lymphoid nodules. In these instances the cells in such an area are either small or round cells, or rather long, irregular cells of an epithelioid type. There are no giant cells present, and the appearance of these nodules does not suggest tubercles. The nodules have apparently no connection with the vascular system of the organ. Besides these nodules, there can be seen occasionally in the liver substance patches of rather diffuse blue-staining material, which, under the high power, are seen to be composed of small rods, presumably bacteria. The hepatic vessels and the bile ducts are apparently normal. In one field one of the bacterial patches described above is present in one of the areas of necrosis, but as a rule no such association exists.

Spleen.—The capsule is not increased in thickness. Trabeculæ appear normal in amount. The Malpighian bodies are rather large, but otherwise show no change. The pulp contains an excess of red-blood corpuscles, which are scattered irregularly among the pulp cells. Some of these can be seen to be inside of large phagocytic cells. In a few places in the substance of the pulp there are sharply localized areas in which the spleen substance has become necrotic. There are present in these areas a moderate number of cells; a few of which are polynuclears, the rest either small, round cells or cells of an epithelioid type. The blood-vessels of the organ present about a normal appearance.

Mesenteric glands.—Show extensive changes in the form of localized or diffuse areas of necrosis. These seem to be most marked in the central portions of the glands, but they are also present in the periphery. The necrotic areas stain rather sharply with the eosin, and contain large numbers of nuclear fragments, some polynuclear leucocytes, and a fair number of round cells and cells of an epithelioid type. In one or two places in the sections there are to be seen diffuse areas of blue-staining which, under the high power, are seen to be made up

of masses of bacteria. These have no connection in any of the sections examined with the areas of necrosis.

Sections of the liver, spleen, kidney and mesenteric glands, stained by Flexner's methylene-blue method, showed masses of bacilli, resembling, morphologically, the typhoid bacillus.

Bacteriologic Examination.—Cultures were taken at the time of the autopsy from the heart's blood, lung, liver, gall-bladder, spleen, kidney and urine. From all of these, with the exception of the kidney and urine, one single organism was isolated which, morphologically, was a somewhat short, moderately thick bacillus which decolorized by Gram's method of staining. It grew upon media as follows:

Agar slant.—Abundant, moist, white, elevated growth.

Blood serum.—A growth very similar in appearance to that on agar.

Potato.—A moist, slight, almost invisible growth.

Bouillon.—A diffuse cloudiness. Hanging-drop preparations show a well-marked motility of the bacillus.

Dunham.—A diffuse cloudiness; no indol reaction could be obtained.

Litmus milk.—After several days it acidified milk, but failed to produce any coagulation.

Gelatin stab.—Moderate white growth along line of inoculation, but no liquefaction of the gelatin.

No gas formation in saccharose, lactose or glucose media.

Cover-glass preparations, stained by Pittfield's method, showed the flagella with a peritrical arrangement. Tested with known typhoid serum, the bacillus produced a typical Widal reaction in 12 minutes with a dilution of 1 to 10; in 42 minutes with a dilution of 1 to 100.

Diagnosis.—Bacillus typhosus.

The cultures from the kidney and urine contained the typhoid bacillus, but associated with an organism giving all the tests for the bacillus coli communis.

The possibility of the existence of typhoid fever without intestinal lesions was long since conceived by Louis[40], who, himself in Observation 52 of his book, reported an instance that during life presented a typical clinical picture of typhoid fever. The patient died on the 55th day of his disease, and the necropsy showed absolutely no existence or evidence of recent implication of the intestinal canal. The belief of the occasional existence of typhoid fever without anatomic intestinal changes was entertained by a number of the earlier clinicians after Louis, but the clinical simulation of enteric fever by other maladies necessarily, in the absence of bacteriologic criteria, makes these reported cases less valuable as contributions to the study of this rare type of typhoid fever. The conclusive demonstration of this form, without intestinal lesions, dates since the discovery of the specific organism of etiologic importance, and more especially from the time when the differentiation of the typhoid bacillus from allied species became more firmly established. In addition to the reported cases of Banti[41], Karlinski,[42] Guarnieri[43], Vaillard[44], Chantemesse[45], and Vincent[46], other instances carrying more conviction have been published by more recent writers.

DuCazal[47], in 1893, reported the case of a young man, 21 years of age, who had been ill for fifteen days before entering the Hospital. The clinical history suggested typhoid fever, subsequently complicated by double pneumonia. At the autopsy the principal lesions were pneumonia of both lungs and acute spleen tumor. The intestines showed absolutely no evidence whatever of any anatomic alterations, but the cultures from the spleen contained bacilli, morphologically similar to, and on media behaving like, Eberth's bacillus. Kühnau[48] some years later published an interesting observation of this kind. The patient was a pregnant woman, 32 years old, who developed typhoid fever with the subsequent development of erysipelas of the face. Bacteriologic examination of the blood during life showed typhoid bacilli, as already mentioned. The woman died, and the post-mortem examination showed enlargement and necrosis of mesenteric glands, abscesses of the kidneys and thrombosis of one of the ovarian veins. The intestines were free from any lesions whatever. The bacillus typhosus was cultivated from the kidneys, mesenteric glands and spleen.

The case of Pick[49] was that of a 23-year-old woman, who died in the fourth week of a typhoid fever. During life the Widal reaction was positive. The anatomic diagnosis of the autopsy was: Typhoid infiltration of the mesenteric lymph glands, parenchymatous degeneration of organs, and left-sided lobular pneumonia. The spleen was not enlarged and the intestines were free from lesions. The serum test after death was positive in 1 to 10; cultures from the gall-bladder and mesenteric glands contained the typhoid organism; that from the spleen was negative.

Meunier[50], at the séance of the Société Méd. des Hôp. de Paris of April 7th, 1897, reported an uncommon observation of typhoid infection in a boy, 8 years of age, suffering from acute miliary tuberculosis. Shortly after admission into the Hospital rose-spots appeared and the application of the Widal test gave a positive reaction. The lesions found at the necropsy were tubercular ulcers of the intestine. Typhoid bacilli were demonstrated in the cultures from the spleen, lungs and pleural exudate.

Beatty[51], about the same time, published a case of typhoid fever, commencing with nausea and pain in the back followed by jaundice. Death on the sixth day. The examination after death showed an enlarged spleen and mesenteric glands, but in the intestines there was an absence of lesions. The spleen contained typhoid bacilli.

Chiari and Kraus[52], in a very recent and valuable article, have discussed the subject very exhaustively and reported seven cases of atypical typhoid infection, in which there was an absence of anatomic lesions of the intestines. These observers classify enteric fever into four great anatomic divisions: The first include all those cases presenting the characteristic typhoid lesions; the second those anatomically atypical but, nevertheless, recognizable cases on the autopsy table; the third comprising that class of cases characterized by an absence of anatomical lesions, making the diagnosis, anatomically, impossible, but in the organs of which typhoid bacilli are found; and finally, the last group to include such cases as cannot be diagnosticated anatomically or bacteriologically, but which give positive serum reaction with the Widal test. Group III, of this classification, is of particular interest to us, inasmuch as the Case II, reported in our paper, belongs to this class. The

typhoid septicæmias frequently fall under this heading. Of the five cases reported by Chiari and Kraus as belonging to this group, only three were based on the presence of the typhoid bacilli in one or more of the organs. The diagnosis of Cases XV and XVI is entirely based on a positive result of the serum test, no typhoid bacilli having been demonstrated in any organ. Although, with proper precautions and in sufficiently high dilutions, the specificity of the serum reaction is almost absolute, nevertheless certain errors must necessarily arise at times, and these become increasingly great as the dilution is made lower and lower. Chiari and Kraus used dilutions of 1 to 10 and 1 to 12, degrees of dilution particularly susceptible to fallacious results. In view of this, Cases XV and XVI lose much of their interest as examples of typhoid fever without intestinal lesions. These remarks likewise, in our opinion, apply with equal force to Case XVIII and all the cases of group IV, the diagnosis of all of which being based on the serum reaction with very low dilutions.

Flexner and Norman Harris (53) very recently have contributed a very carefully studied additional example of typhoid infection without intestinal lesions. The case was that of a man, 68 years of age, who suffered from shortness of breath, symptoms of pleuritis, and finally died two days after admission into the Hospital. The autopsy, performed one hour after death, showed thrombosis of pulmonary artery, gangrene of lung, perforation of pleura, pyo-pneumo-thorax, acute spleen tumor, parenchymatous degeneration of liver and kidneys. The mesenteric glands were not swollen, and the intestines showed nothing abnormal. The bacteriologic examination demonstrated the presence of typhoid bacilli in liver, spleen and lung.

Examples of typhoid fever, without intestinal implication, are not entirely limited to adults, but, on the contrary, the apparent small disposition to intestinal lesions of very young children suffering from this disease is one of considerable interest in this connection. Chantemesse and Widal (54) called attention to the trivial character of the intestinal lesions in the young some years ago; and Brouardel and Thoinot (55) likewise mention this peculiarity, as does also Marfan (56). The publications of Etienne (57), Freund and Levy (58), and others, include cases of this character in which the intestinal lesions were at a minimum or totally absent.

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CAVITIES IN THE BRAIN PRODUCED BY THE BACILLUS AEROGENES CAPSULATUS.

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Reports of cases of subcutaneous and visceral invasion by gas-forming bacilli are multiplying rapidly. Chas. Norris[1] has given the most recent monograph on general infection by the bacillus aerogenes capsulatus. He reviews most of the recent literature and enters especially into bacteriological experimentation. The following case is of interest because the bacilli seemed to have had a predilection for the brain.

HISTORY OF CASE.

Mrs. C. B. Age, 35. Colored. Admitted to the Surgical Ward of the Maryland General Hospital, suffering from shock caused by a gunshot wound of the abdomen. Prof. J. D. Blake was summoned and performed a laparotomy, suturing several perforations of the intestine. The bullet was not found. After applying the dressings the patient was put to bed and rallied from the operation very well. There was a slight rise of temperature the first day, but this soon subsided and it seemed as though an uneventful recovery would ensue. There was no pain or distention of the abdomen. Temperature and pulse normal, bowels constipated. On the third day a change in her condition was noticed. She seemed to be getting weaker without any appreciable cause. In a few hours after the change was noticed she quietly passed away. At the autopsy, which was performed 24 hours after death, the following condition was found: Body that of a strongly built and well-nourished negro woman. Rigor mortis marked. No crepitation of subcutaneous tissue. On opening the abdominal cavity the viscera appeared normal. The perforations were healing nicely; no indications of peritonitis. The bullet was found in left iliac muscle. On section of the various organs there were no appreciable signs of gas formation except in the uterus. Here a number of small spaces were seen. No gas could be detected, and on microscopical examination no bacilli were found. The heart and lungs were normal. The dura mater was found closely adherent to the calvarium. The brain was removed, surrounded by its meninges, and placed in a 4 per cent. solution of formalin to harden, before sectioning. The spinal cord was not removed. The external aspect of the brain was normal, the sulci and gyri being especially well marked. After the brain was thoroughly hardened (4 to 6 days), horizontal sections were made from the base upward, which revealed the following condition:

In the right hemisphere there existed a large cavity, involving the external capsule in its entirety, being five centimeters long, one centimeter broad and two centimeters deep, which appeared to be lined by a smooth glistening membrane. A small amount of bloody serum was found in it. Throughout the lenticular nucleus numerous small cavities were found, varying from one-half to one centimeter in extent. The anterior limb of the internal capsule, on a level with the middle commissure, contained several cavities, also a small one in the optic thalamus. Another section made on a level with the velum interpositum showed the posterior limb of the internal capsule to be almost completely destroyed by two large cavities. None of these spaces communicated with the ventricles. The caudate nucleus was intact. In the external orbital convolution a large cavity existed, being three centimeters deep and one centimeter broad, apparently lined by a smooth membrane.

Left hemisphere was smaller than the right. The first section revealed a cavity in the anterior limb of the external capsule two centimeters long and one centimeter deep. In the posterior limb 3 to 6 small pits or depressions were seen. In the lenticular nucleus several large excavations. The fibres of the internal capsule on this side seemed to pass around the cavities. The caudate nucleus and optic thalamus were normal. The cavities on this side were not as large nor as extensive as on the opposite side. The sulci and gyri were especially well marked, the former being very deep. No cortical or subcortical lesions were found. On section the cerebellum showed a few small subcortical cavities in the arbor vitae, superior surface. Otherwise, it was normal. After seeing this honeycombed appearance of the basal ganglia, the question immediately arose as to the cause. Was it congenital or acquired? Could the woman have lived in this condition without manifesting any symptoms of cerebral trouble? Could it be porencephalia? Was it produced by formaldehyde? These and numerous other surmises were not answered until sections were made and examined microscopically.

We submitted several sections to Dr. Barker, who at once recognized the bacteria as the cause of the cavity formation.

On studying sections under the low power of the microscope, the edges of the cavities appear quite smooth, and the clean-cut appearance seen in the gross sections of this brain again shows itself. They are devoid of any membranous or epithelial lining. Indeed, some of these cavities are surrounded by comparatively normal tissue, the brain cells in some instances forming the very edge. This is, however, an exception; for surrounding most of them is an area of cell degeneration of variable thickness, which is easily recognized by the absence of nuclear staining; indeed, the absence of all cellular structure is frequently seen in this zone, so that a diffuse homogeneous staining with eosin divides this from the zone to be described next. On passing outwards, this advanced stage of degeneration is gradually superseded by one in which only a partial loss of nuclear staining is evident and staining of the individual cells appears. Lastly, this zone merges into normal brain tissue. As for the spaces themselves, they are usually quite empty, excepting for certain masses which take on a deep hæmatoxylin staining and under the low-power lens have a somewhat granular appearance; not infrequently these masses lie imbedded in the

walls of the cavities; but what is especially striking, is that by far the majority of the capillaries in the section are completely filled by them. When examined under a higher lens (No. 7 or oil immersion), it becomes evident that these darkly staining masses, just mentioned, represent aggregations of bacilli, and, as far as we can judge from microscopical appearances alone, they are pure growths of a bacillus having the following morphology:

A fairly long, rather thick, bacillus, varying at times in either dimension, at times in both, with an average length from 3 to 6 mm., and with the comparative thickness of the anthrax bacillus; its ends are slightly rounded; the organism occurs singly, in pairs and clumps, and in parts of these specimens as chains. It stains with the ordinary aniline dyes; also by Gram's method. No spores were found, but no special stain was used for their demonstration. The bacilli frequently lie free in the tissues at some distance from cavities, and their clumps are almost invariably surrounded by zones of cellular degeneration, such as have been described surrounding the cavities; similar cellular changes are frequently seen in the neighborhood of bacilli which lie within blood-vessels. Judging from these specimens it would seem that the veins and capillaries are especially active in carrying the organism, for those arteries with well-marked walls showed as a rule, with one or two exceptions, no bacilli in their lumina. As to the part played by the lymphatics in such a conveyance it is difficult to say; we believe they played a minor rôle in this case. In none of the perivascular lymph spaces (space of His) could we find the organism.

In no portion of the specimen were there any changes pointing to an inflammatory reaction, the entire absence of small-cell infiltration being very striking.

There are no hemorrhages in the brain tissue, nor could we detect the presence of blood in the cavities.

The arteries throughout are normal, showing no evidence of sclerosis. Any attempt at repair was entirely wanting, there being no neuroglial hyperplasia nor formation of granulation tissue.

CONCLUSION.

We believe that the cell degenerations and cavity formation in this case are due to the presence of the bacilli described, and that they belong to the class of gas-forming bacteria, the gas formation being directly responsible for the presence of the cavities, and the cellular changes being due to the action of toxins.

In 1892 Welch and Nuttall[2] reported in the July-August number of the Johns Hopkins Bulletin their discovery of a gas-forming bacillus obtained from the emphysematous tissues and blood of a man dead of aneurism of the aorta, for which they proposed the name, bacillus aerogenes capsulatus. Gas bubbles were abundantly present in the internal organs, notably in the myocardium, the liver, spleen and kidneys. This gas burned with a pale-bluish, almost colorless flame, a slight detonation being heard at the moment of ignition.

Upon microscopical examination of these organs, they found around masses of bacilli frequently, but not always, a disappearance of the nuclei and degenerative changes in cardiac muscle cell, and the epithelial cells of the liver and kidney, especially in the neighborhood of gas cavities, in the walls of which the bacilli were often densely accumulated.

They describe the bacillus aerogenes capsulatus as follows:

The bacillus is non-motile, straight or sometimes slightly curved, variable in size, but averaging about the thickness of the anthrax bacillus, and from 3 to 6 cm. in length, with adjacent ends slightly rounded or sometimes square cut; occurs singly, in pairs, in clumps, and sometimes in chains, and stains readily with the ordinary aniline dyes, and after using Gram's method, staining is either uniform or with small unstained spots, less frequently with isolated deeply staining granules.

Capsules, although not constant, were frequently demonstrated, especially by Welch's method for staining capsules in specimens from the animal body and sometimes from agar cultures. No spores were found either in the animal body or in cultures.*

The bacillus grows upon all ordinary culture media under anaerobic conditions, at body temperature slowly; at 18 to 20 C. no growth on surface of solid media under ordinary conditions. Gas is produced in all cultures containing fermentable material. Time and space will not permit us to describe the cultural characters more in detail, and those interested in this subject are referred to the original paper and also to that of Welch and Flexner in the Journal of Experimental Medicine, Vol. I. This organism is non-pathogenic to rabbits even when a pure culture is injected into the circulation.

If the animal is, however, killed immediately or soon after intravenous injection, after 4 to 6 hours at 30 C., or about 18 hours at 18 or 20 C., there follows great gas formation in the blood-vessels and organs and the bacilli are found abundantly in these tissues.

Although we cannot prove in the absence of cultural growths of the organism found in this brain that the bacillus under consideration is identical with that described by Welch and Nuttall, there seems to be little doubt from the resemblance in morphology, staining characteristics and more especially in its reaction to Gram's method, and last but not least, in the changes which it produces in the tissues, that this organism is at least closely allied to the bacillus aerogenes capsulatus and probably identical. As animal experiments show this organism to be non-pathogenic, and clinical experience, with a single exception, tends to show that general infection with this organism takes place immediately before or after death, practically the latter only, as far as can be judged from the symptoms due to general gas formation in the body; and further, as there is no evidence in this case which points to a general infection by this organism, before the death of the individual, we concluded that the changes occurred post mortem, the distribution of the organism most likely occurring in the preagonal period. The organism not infrequently produces localized emphysematous conditions only in the tissues, from which recovery usually takes place because it seems essential for the existence and growth of this organism

* Since this publication Dunham has found that this organism produces spores when grown on blood serum.

that the tissues must have been previously injured or that the blood-supply should be poor in oxygen. That an injury may be trivial and still favor its development seems quite clear from two cases reported by Fraenkel,[3] in which infection followed hypodermic injections, in one case after the injection of camphor, oil and ether under the skin, and in the other of a dilute solution in water of sulphuric acid and chloride of morphia. One of these cases pursued a rapidly fatal course, death occurring two days after the injection. Before the discovery of this organism the cause of death in such cases would very likely have been attributed to the entrance of air into a vein. Welch and Nuttall in their original paper expressed the belief that many of the deaths attributed to the entrance of air into the veins would prove to be cases of gas bacillus infection, and especially referred to cases occurring in obstetrical practice in which it was supposed that air had entered the uterine cavity and had been absorbed by the uterine sinuses thus causing fatal air emboli. Perkins[4] reports such a case following an attempt at criminal abortion, and attributed the fatal outcome to air embolism. Dr. Dobbin,[5] of the Johns Hopkins Hospital, through the kindness of Dr. Perkins, had an opportunity of studying sections from the uterus in this case and found the characteristic lesions of gas bacilli infection, the bacilli corresponding in morphology and staining characters to the bacillus of Welch and Nuttall.

The "Schaumorgane" of the Germans are due to such infections and the elaborate article of Ernst[6] on the "Schaumleber" is especially rich in the microscopical changes in the tissues. He describes the microscopical appearance of the "Schaumleber" as follows: "On making the usual single long transverse section through the liver, the two portions thus formed fell apart almost immediately, and while examining these gas bubbles I saw that they began to appear from the larger vessels soon in such numbers that hillocks of froth were formed on the surface of the section; these hillocks gradually coalesced. If these masses of froth were stripped away, hardly a few minutes passed before fresh ones had formed. This condition of re-formation of froth continued for a long time. The autopsy had been performed 3 hours after death and there were no evidences of decomposition."

In reviewing the literature on this subject one clearly sees that these infections with gas-forming bacteria are becoming more widely recognized, and the number of articles have increased every year since the appearance of those of Welch and Nuttall and that of Ernst. In fact, at present the changes due to these bacteria have been described in almost every organ, including, for instance, the liver, spleen, stomach, intestines, bladder, kidney, uterus, skeletal muscles, etc. Notwithstanding this, we have been unable to find any description of pathological changes attributed to these bacteria in the brain or spinal cord, which seems indeed strange if one considers the comparative frequency of these infections and that they are fairly well recognized by observers in general. One can hardly believe that the central nervous system should be spared from such changes in cases of general infection where almost all organs may show the presence of gas cavities. Of course that the liver, spleen, and perhaps the uterus may predominate in showing the presence of these cavities when once the general circulation conveys the organism is not difficult to understand, for as the veins seem to be especially employed in such a conveyance it is no more than natural that organs which are abundantly supplied with large veins and therefore containing a large amount of the blood after death would contain a relatively greater number of the organism than an organ in whose parenchyma the veins were less abundant and the venous radicles of small calibre. The brain and cord can certainly be classed with those organs possessing a comparatively small amount of blood in their parenchyma after death; of course the membranes covering them must be excluded, for in these the veins being large, and containing a large amount of blood, in all probability an examination would, in the great majority of instances of general infection, reveal the presence of the organism. Of course the smaller venous radicles of the brain parenchyma would also contain a fair number of the organism, but these might be present in insufficient numbers to produce sufficient gases to give rise to appreciable microscopical lesions. We refer here, of course, more especially to cavity formation. The above is only a theory intended to cover the inference that probably in a great number of cases of gas bacillus infection showing gas cavities throughout the organs, the brain and spinal cord will in the great majority be spared. But in looking over the articles on this subject one can easily see why such changes in the central nervous system should have been overlooked and that in the report of cases coming to autopsy we have been unable to find, with one or two exceptions, any mention of a removal of the brain or cord, and it is more than likely that this was neglected, for had they been examined mention of this fact would undoubtedly have been made—this of course is a very evident reason for the non-recognition of similar changes as are described in this brain. Although this is, as far as we know, the first case in which cavity formation has been attributed in the brain to the presence of gas bacilli we do not claim that such changes have not been described before, but they have been explained by different etiological factors. Of such an instance we have found but two clear examples; both the brains are described by the same observers, namely, by G. H. Savage and W. Hale White, in an article entitled "Causes of Holes in the Brain," appearing in the Transactions of the London Pathological Society, Vol. XXXIV, 1882. These brains the authors obtained from two general paralytics, and as the kidneys, liver, lungs, and heart muscles contained cysts, they very naturally describe the changes by the term of "Universal cystic degeneration." In reading this article one is struck with the admirably clear description of the pathological changes. The illustration of the brain presented herewith shows a picture almost identical with the one reported by us, so that we feel little hesitancy in ascribing the changes described by Savage and White to the bacillus aerogenes capsulatus or an allied organism. A short résumé of the description of the brains and the changes in the other organs will not be out of place.

"Taking first the kidney, sections appear to show that in our cases .... the cystic change is due to dilatation of either the Malpighian capsules or cortical tubules. And in the liver .... the cysts appear to be due to small vacuoles in the

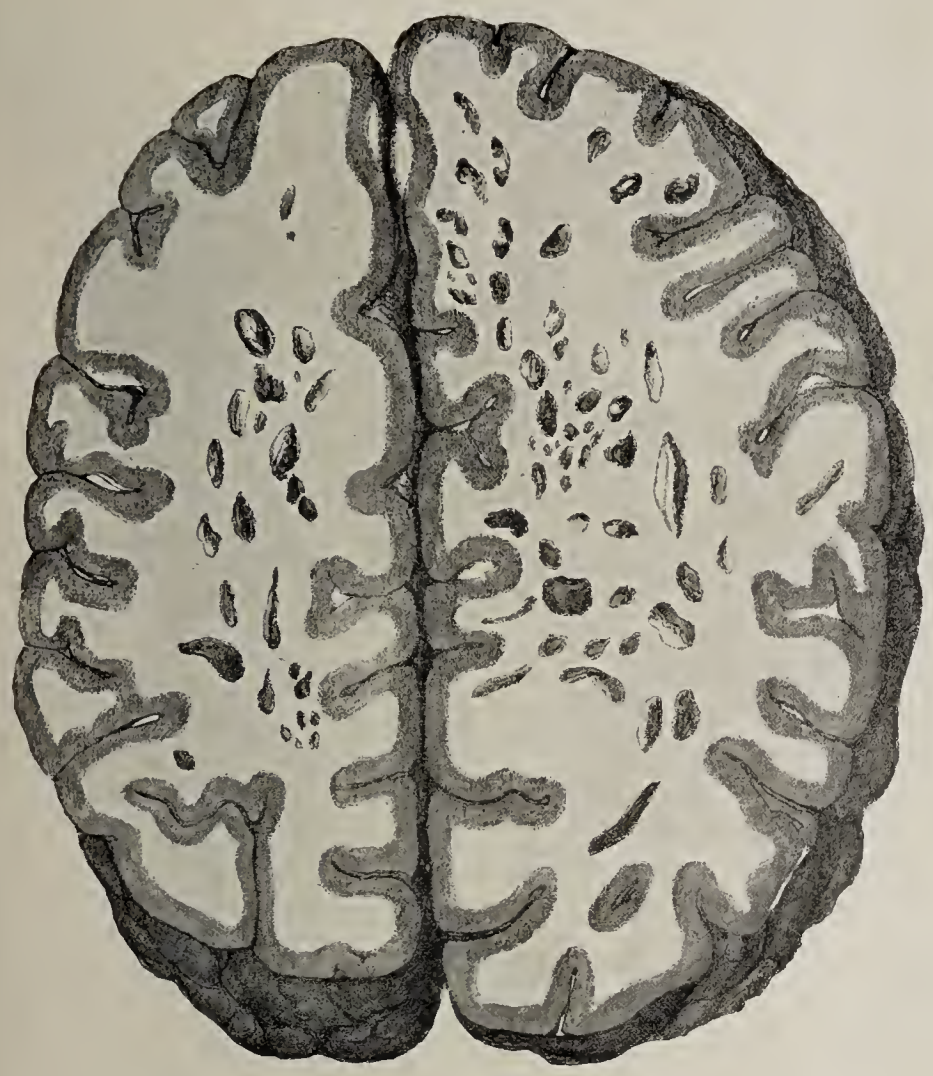


Fig. 2.—Reprodnction of section of brain from Hale White and Savage's case of "General Cystic Degeneration." [Transactions of Pathological Society of London, Vol. XXXIV.]

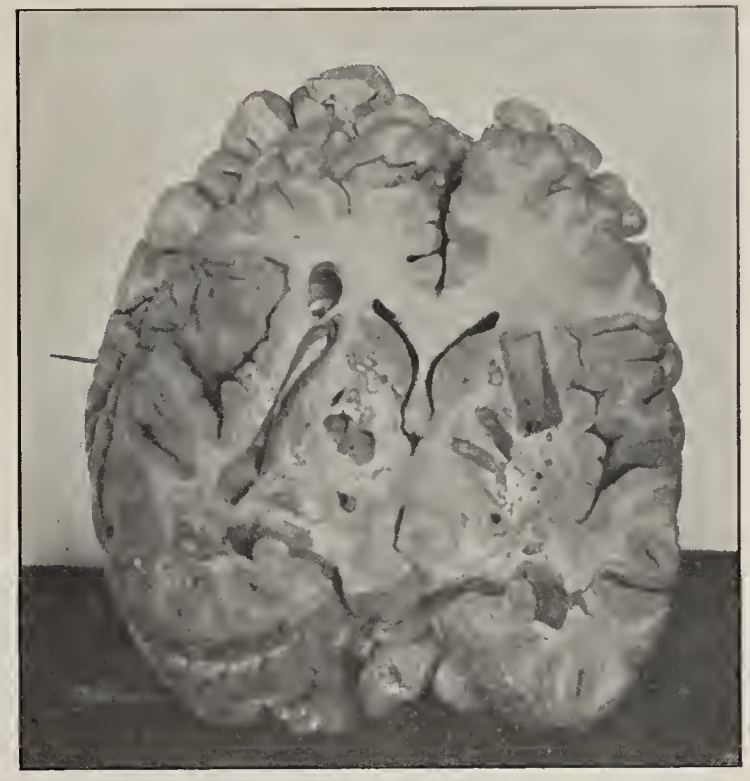


Fig. 1.—Photograph showing cavities in the corpus striatum.

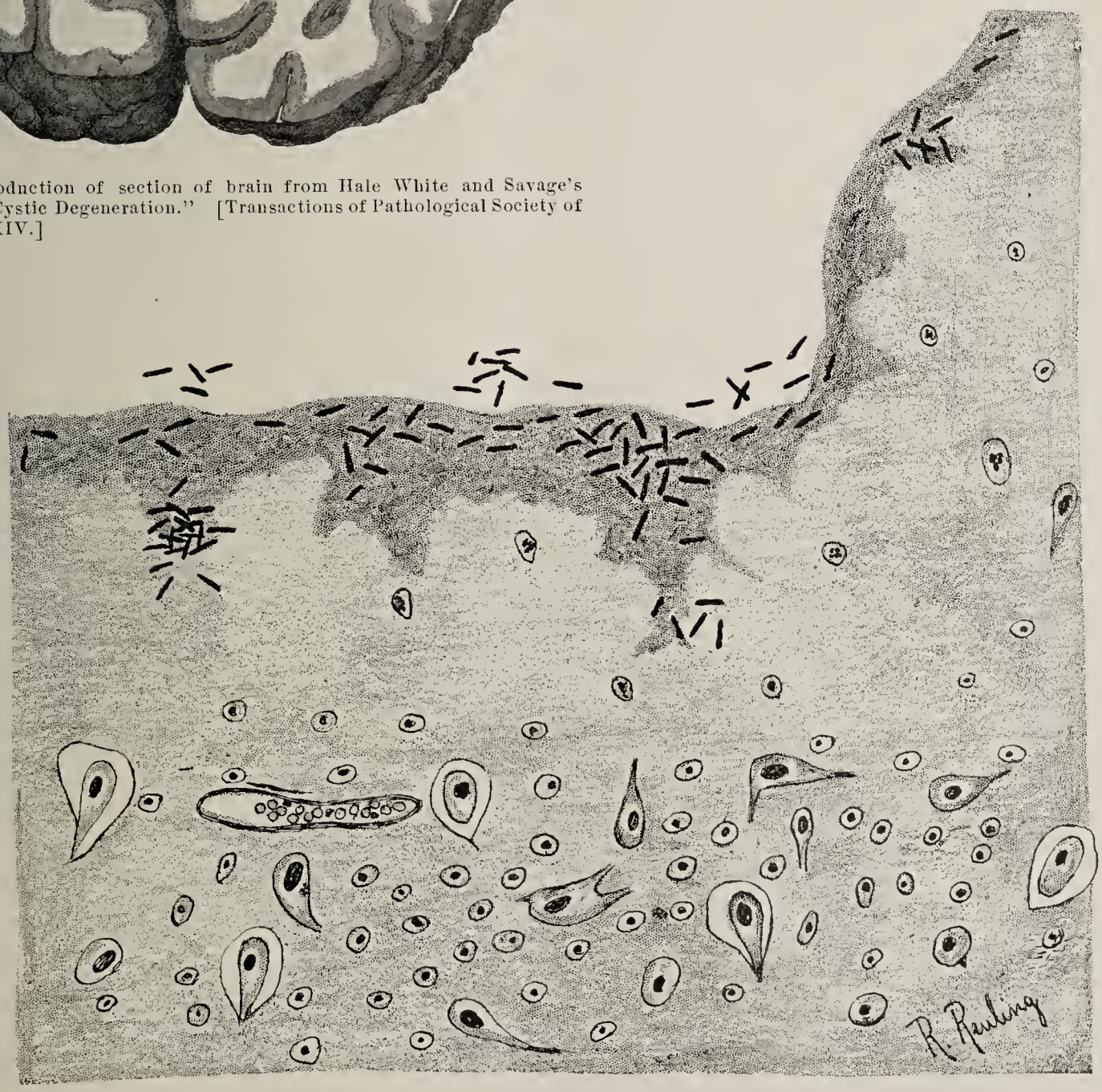


Fig. 3.—Section showing edge of large gas cavity with bacilli in its walls. Surrounding this is an area of cellnlar degeneration. (Immersion lens.)

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hepatic cells, which we have proved not to be fatty by their refusal to stain with osmic acid. The several vacuoles in the same cell, by increase in size, run together to form one that occupies nearly all the cell, which being so distended bursts. The vacuoles of adjacent cells thus coming together soon form one large cyst. . . . . By this process in parts of the liver the cysts produced are so numerous that the whole organ has the appearance of a sponge; this is very well shown on holding up one of the microscopic slides. . . . . We do not think the hepatic cysts have any true wall, but the appearance of one is often produced by the cyst in the course of its enlargement coming in contact with some fibrous tissue, which it stretches and pushes before it, so that at last it appears to have a thin lining membrane."

"*Lungs*—The cavities are mostly circular and not connected with bronchial tubes; they contain no lining membrane. They have a tendency to occur in groups, and seem to be situated indiscriminately among the air-cells, from which they are distinguished by their regular shape and containing no granular epithelial debris, but in many cases the cysts have in the interior a peculiar amorphous matter which takes the logwood stain with great brilliancy."

Before going any further we wish to call especial attention to the mention of this "amorphous matter" which takes on the logwood stain so deeply, which the authors describe in the cavity of the brain and in the vessels of the different organs; this seems especially important as this "amorphous matter" which they describe is undoubtedly composed of masses of bacteria which the reader will remember often completely filled the vessels in the brain we describe and were so abundant in the walls of the cavities. Savage and White give only a short description of the appearances of the brain, but substitute for this a good illustration of the specimen. The description of the microscopical appearances of the brain cysts corresponds in all particulars to those found in the other organs. It would be useless for us to go into a minute comparison of the changes described in the case reported in this article and the other pathological conditions giving rise to cavity formation in the brain. One could hardly, after a careful consideration of such conditions as porencephalia which has been so admirably treated by Kundrat[7] to which the reader is referred—the condition known as *état criblé*[8]—is now considered by most observers as of no pathological significance and the holes in this are extremely small, generally of pin-point size and are frequently due to slight dilations of the Virchow-Robin lymph space, or by a shrinkage of the brain substance from the action of hardening fluids, causing a rather wide separation between vessels and parenchyma.

The holes produced in sclerotic processes found at times in the brain of general paralytics, and patients suffering from multiple sclerosis, could hardly take a form to resemble those cavities produced by this organism, as the former would almost necessarily contain a lining membrane, and evidences of neuroglial hyperplasia in different localities would speak for the chronicity of the process.

Discussion.

Dr. Welch—In connection with Drs. Herring and Reuling's contribution, it may be of interest to exhibit a microscopical section from a pig's liver which I examined to-day. I received the section from an eminent pathologist who was puzzled by the appearances. Two or three of the superficial lobules of the liver presented to the naked eye small, bleb-like spaces. The sections show a honeycombed appearance of the affected lobules, caused by an abundant development of bacilli identical, morphologically, with the B. aerogenes capsulatus. The gaseous spaces are sharply defined, and the appearances are indeed such as to be very puzzling, unless one is familiar with the blebs produced by the post-mortem development of our gas bacillus. The specimen is an example of emphysematous liver (Schaumleber), but is remarkable on account of the limited production of gas and the circumscribed arrangement of the holes, due in part to the large amount of connective tissue normally surrounding the hepatic lobules of the pig.

In the light of Drs. Herring and Reuling's observation, it is probable that certain cases reported in the literature as holes in the brain are really due to the post-mortem development of the gas bacillus.

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ACUTE FIBRINO-PURULENT CEREBRO-SPINAL MENINGITIS, EPENDYMITIS, ABSCESSES OF THE CEREBRUM, GAS-CYSTS OF THE CEREBRUM, CEREBRO-SPINAL EXUDATION, AND OF THE LIVER, DUE TO THE BACILLUS AEROGENES CAPSULATUS.

By W. T. Howard, Jr., M. D., *Professor of Pathology in the Western Reserve University, Pathologist to Lakeside Hospital, Cleveland, Ohio.*

(*From the Pathological Laboratory of Lakeside Hospital.*)

For the clinical history of the following case my thanks are due to Dr. Dudley P. Allen. H. E., male, white, aged 31 years, was admitted to Lakeside Hospital, service of Dr. Allen, March 22, 1898. His family history was without interest. The patient had had chicken-pox and scarlet fever, but denied syphilis.

In August, 1897, he contracted gonorrhœa, and shortly after this he noticed a painful swelling in the perineum. Six months later this ruptured, with the discharge of a considerable amount of pus. After this there was a permanent urinary fistula at this point. Three months after the occurrence of the first swelling another formed in the same region, and after the escape of pus healed and disappeared.

With the usual precautions under ether anæsthesia Dr. Allen curetted the fistulous tract which communicated with the urethra. After dilatation of the urethra a catheter was inserted and the wound allowed to heal.

A few days after the operation the patient became unconscious, developed symptoms of meningitis and died during the night of March the 29th, 1898. After the operation the temperature ranged between 99° and 104°, reaching 105° F. before death.

A few minutes after death the body was placed in a cold-storage chest kept constantly at 32° F.

The autopsy was begun ten hours after death.

Anatomical Diagnosis.—Operation for cure of perineal fistula. Acute fibrino-purulent cerebro-spinal meningitis and ependymitis, with abscesses of the cerebrum, gas-cysts in the cerebrum, cerebro-spinal exudation and in the liver, septicæmia (?), due to the bacillus aerogenes capsulatus; fatty degeneration of the liver, heart and kidneys; cloudy swelling of the kidneys.

The body was 182 cm. long, the surface cold, rigor mortis was marked. There was no œdema and no emphysematous crackling of the subcutaneous tissues. The abdominal muscles were well developed. The peritoneum was smooth and glistening. The pelvic cavity contained a small amount of slightly blood-tinged fluid with a few gas bubbles. The abdomen was not distended.

The chest was well shaped. The pleural cavities and the pleuræ were normal.

Both lungs were enormously congested and showed small areas of consolidation. On section a large amount of dark fluid-blood containing gas bubbles escaped. Gas bubbles escaped from the pulmonary vessels on pressure. The mucous membrane of the bronchi was deeply congested. The lungs were moderately pigmented. The bronchial glands were pigmented, but were free from tuberculosis. The mucous membrane of the trachea and larynx was congested.

The pericardium was negative. The heart was of ordinary size. The myocardium was pale. In the right auricle and auricular appendage and the right ventricle there were dark fluid-blood and loose clots, with a large number of large and small gas bubbles. The valves and coronary vessels were normal.

The liver was of ordinary size and its capsule smooth. On section a large amount of dark red blood containing large and small gas bubbles escaped from the hepatic and portal veins. The lobules were well marked; the consistencies were not specially increased. Scattered throughout the organ there were a large number of small opaque areas the size of a pin's head. The bile-ducts and the gall-bladder were negative.

The spleen was four times the ordinary size. The capsule was not thickened. On section the organ was soft, dark red in color and markedly hyperæmic. The Malpighian bodies and the trabeculæ were obscure. A large number of gas bubbles escaped on section.

The kidneys were of ordinary size. The capsules were readily removed. The surfaces were pale. The cortices were somewhat thicker than ordinary, and the glomeruli and veins were markedly congested. There were no gas bubbles to be found in the kidneys. The adrenals were negative.

The pancreas, œsophagus, stomach and small intestines were markedly congested. The colon and rectum showed nothing of interest. The testicles were negative. The urethra was normal; there was no strictnre to be found. The perineal wound was healed, and no pus and no gas bubbles could be found. The right lobe of the prostate was larger than ordinary. No abscesses were found. The bladder was distended with urine. The mucous membrane was moderately congested; there were no ulcers. The pelvis was deep and narrow. Careful dissection failed to show any focus of suppuration. The pelvic veins, the inferior vena cava and the portal vein all contained large and small gas bubbles.

Head.—The scalp was of ordinary thickness and moderately congested. The skull was normal. The vessels of the dura-mater were moderately congested. The sinuses contained dark fluid-blood with large and small gas bubbles.

Brain.—The vessels of the surface of the brain were very much congested. The pia-arachnoid over the cerebral hemispheres showed a number of small opaque areas of fibrinous exudation. The structures at the base of the brain, including the nerves, were bathed in a thick yellow pus. The pia-arachnoid over the inferior surface of the cerebrum, a large portion of the cerebellum, the pons and the medulla were covered with a thick fibrino-purulent exudation.

On section of the left cerebral hemisphere just above the

Sylvian fissure, involving the intra-parietal fissure, and the ascending parietal and the supra-marginal convolutions, there was an abscess with soft, necrotic walls. This abscess varied from 0.5 to 2 cm. in diameter. Near this abscess at one side there were a number of smooth-walled cavities measuring from 1 to 5 mm. in diameter.

On the inner side, this abscess extended deep into the tissue. Occupying the anterior half of the left superior tempero-sphenoidal convolution there was an irregular abscess with soft necrotic walls. The abscess cavity was filled with a semi-fluid necrotic material. This abscess varied from 0.5 to 1.5 cm. in diameter. Both of these abscesses extended inwards and communicated with the left lateral ventricle. Nearly the whole of the surface of this ventricle was covered with a thick layer of pus and the wall over a large surface was necrotic. The lenticular nucleus of the left side contained a number of small smooth-walled gas-cysts or cavities varying from 1 to 5 mm. in diameter. In the internal capsule there were several similar gas-cysts. The right lateral ventricle, the right cerebral hemisphere, the cerebellum and the pons and medulla showed nothing abnormal on section.

Spinal Cord.—The dura mater was moderately hyperæmic. The vessels of the pia-arachnoid were hyperæmic and contained small gas bubbles. In the membranes there were gas-cysts from 1 to 3 mm. in diameter. The cord was of ordinary consistence and appeared normal.

Bacteriological Examination.—Coverslip preparations made from the lungs, heart, venæ cavæ, portal vein, pelvic veins, liver, the cerebral and spinal exudations, and the brain abscesses, showed in great numbers and in pure culture a large stout bacillus often in pairs, threes and fours end to end, and usually with capsules. Careful study of the meningeal exudate failed to demonstrate the presence of any other bacteria. Half a cubic centimeter of this pus was injected into the ear-vein of a rabbit. The animal was killed a few minutes later and put in the incubator. After five hours the animal was enormously swollen, its subcutaneous tissues being emphysematous. At the autopsy gas was found in the heart and blood-vessels and in all the organs. Capsulated bacilli similar to those injected were found in pure culture in the various organs.

At the autopsy plate and slant cultures were made on glucose agar and upon slanted coagulated blood serum from the brain abscesses, the meningeal exudate, the heart's blood, and from the liver, lungs, spleen, kidneys and portal vein, were grown both aerobically and anaerobically (Novy's jars).

The aerobic cultures were sterile after three days in the incubator. All the anaerobic cultures showed, after 24 hours in the incubator, numbers of grayish-white colonies, which after a few days were from 2 to 3 millimeters in diameter. In gelatine cultures slow liquefaction of the medium occurred. Milk was coagulated in forty-eight hours. There was slight visible growth with gas formation on potato. Sugar bouillon was rendered diffusely cloudy. The organism was non-motile. In blood serum-cultures spores were found.

The bacillus produced gas in media containing fermentable substances. Cultures of this bacillus were pathogenic for guinea-pigs and pigeons. Rabbits killed after intravenous inoculation and kept in a warm place always showed marked emphysematous swelling with typical "Schaumorgane." This bacillus stained well with the aniline stains and by Gram's staining method.

From the brain abscess and the meningeal exudate, then, as well as from the various organs there was obtained in pure culture a bacillus identical with the bacillus aerogenes capsulatus (Welch).

Microscopical Examination of the Organs.

The brain and spinal cord were hardened in 10% formalin, and portions of the other organs were hardened in Zenker's fluid and in 95% alcohol.

Central Nervous System.—Sections made from the cerebral and cerebellar cortex, from the pons and medulla and from the spinal cord, and from the brain abscesses were stained in hæmatoxylin and eosin, in eosin and methylene-blue, in thionin, and in carmine followed by Weigert's fibrin stain. A study of the meningeal changes showed marked dilatation of the blood-vessels. Many of the small arteries were filled with both polymorphous and mononuclear leucocytes. In some vessels the endothelium was partially or totally desquamated and the sub-endothelial tissue infiltrated with cells, and well marked thrombosis was found in some arteries. In some vessels both polymorphous and mononuclear leucocytes could be seen in the media and adventitia. In some places there was proliferation of the cells of the adventitia with the formation of large round or spindle-shaped cells. Only a few bacilli were seen in the vessels, but in places numbers were found in the adventitia. The exudation varied very much in thickness, being thickest at the base of the brain over the cerebellum, the pons and the medulla. The most numerous cells were polymorphous nuclear neutrophiles. Besides these there were many mononuclear cells of varying size and answering to the description of plasma cells. In addition to these in some places large round or oval mononuclear cells of the connective-tissue type were seen. Here and there a few red-blood cells were found. In some places the exudation was rich in fibrin, while in others this was scanty.

In many places on the cerebral and cerebellar cortex, proceeding along the course of the vessels in the *sulci*, there was a marked infiltration with polymorphous nuclear leucocytes and plasma cells. The exudation was, in general, rich in fibrin. The blood-vessels were dilated, and many of the arteries showed the same changes described in the meningeal vessels. In these areas bacilli were always found. In some of these broad bands of cellular infiltration in the cerebellum gas-cysts of varying size containing bacilli were seen.

Sections of the cord made at different levels showed well-marked meningitis. The exudation was most marked in the cervical and upper dorsal regions, and was in every way similar to that described in the cerebral meninges. At various places, especially, however, in the exudation over the medulla and the cervical cord, there were a number of gas-cysts. The gas-cysts of the spinal meninges varied from twenty μ to four to five mm. in diameter. The cysts of the pons and medulla did not exceed one hundred μ in diameter. These cysts were round or oval in outline and contained, both in their cavities

and along their margins, a number of large bacilli. The exudate in the neighborhood of the cysts was usually compressed.

Brain.—Sections made through the abscesses in the supra-marginal and ascending parietal convolutions and including the intra-parietal tissue, and through the abscess of the superior tempero-sphenoidal convolution showed large central areas of necrotic material. This material was homogeneous and hyaline in appearance and stained diffusely with eosin. Here and there a few nuclei could be made out. Nuclear fragments were numerous in some places. In this material myriads of bacilli were found. The bacilli occurred singly and in small and large groups. About the necrotic area there was always a deep zone of dense cellular infiltration. The most numerous cells were polymorphous nuclear leucocytes. Lymphocytes and plasma cells were found in great numbers. Many of the cells resembling plasma cells contained two nuclei and were evidently proliferating. In some places cells with kidney-shaped nuclei were seen. This zone of cellular infiltration varied from one to three or four mm. in thickness. Bacilli in small and large groups, sometimes in huge clumps, could always be found in this zone. Infrequently bacilli were found in leucocytes. The blood-vessels near this zone were dilated. In many of the arteries among the red-blood cells many polymorphous nuclear and large mononuclear cells were seen. In some vessels thrombi were found. In these the intima cells were often desquamated and leucocytes were seen in the media. Well-marked cellular infiltration was found about many of the arteries. Bacilli were but rarely seen inside the vessels. Near the zone of cellular infiltration a varying number of bacilli were sometimes noticed. In rare instances in this region small spaces (gas-cysts), varying from ten to thirty μ in diameter and containing bacilli, were found.

In sections including the wall of the left lateral ventricle no trace of the ependyma remained. The ventricular surface of the sections was covered with a thick layer of hyaline material staining diffusely with eosin. This hyaline, homogeneous layer varied in thickness, and was similar in appearance to the necrotic material of the abscesses of the cortex. This layer contained myriads of bacilli and often nuclear fragments, with an occasional polymorphous nuclear leucocyte. Beneath this layer there was a thick zone of cellular infiltration in every way similar to that described in the abscesses. Many bacilli were seen among the cells in this zone. The underlying tissue showed areas of infiltration with cells about the blood-vessels, many of which contained thrombi. With the exception of the gas-cysts and the inflammatory lesions above described, no special changes were made out in the white or gray matter of the brain or cord.

Sections of the gas-cysts or cavities in the internal capsule and in the lenticular nucleus showed simply separation and compression of the tissues due to the pressure exerted by the gas. None of the cysts appeared to be dilated blood-vessels. Large numbers of bacilli were always found along the walls of the cysts. In some places large clumps or colonies were to be seen. There was no inflammatory reaction about the cysts.

Four varieties of gas-cysts could be recognized in the central nervous system in this case. (1) Cysts developed in the meningeal exudation on the surface of the cerebrum, cerebellum, pons, medulla and spinal cord. These cysts varied from twenty μ to from two to five mm. in diameter. (2) Small cysts, never exceeding fifty μ in diameter, occurring in the inflammatory exudation following the course of the arteries in the cerebellum. (3) Small cysts from ten to twenty μ in diameter, occurring near the abscesses in the parietal lobes. (4) Cysts varying from 0.5 to 1.5 mm. in diameter found in the superior tempero-sphenoidal lobe, in the lenticular nucleus and internal capsule on the left side.

Lungs.—Sections of the lungs showed slight chronic interstitial pneumonia and emphysema. There was marked congestion of the air vesicles about some of the small bronchi. No bacilli were seen in the alveoli or in the blood-vessels, though some of the latter contained many leucocytes.

Liver.—The liver showed extensive fatty degeneration, best marked in the liver cells at the periphery of the lobules. The interlobular fibrous tissue was increased, and in many places was infiltrated with cells resembling lymphocytes and plasma cells. Nuclear figures were occasionally seen in the latter cells. The veins and capillaries were congested and in many bacilli were seen. In a number of sections there were areas varying from 0.5 to 1 mm. in diameter, in which the nuclei of the liver cells did not stain. The cytoplasm was swollen and more granular than ordinarily. Many cells contained fat drops. Many of the liver cells, especially in the centre of the areas, were shrunken to one-half their normal size. In these areas the endothelial cells of the capillary walls did not stain. Occasionally leucocytes still retaining their staining properties were seen. Long stout bacilli were always found, sometimes in small, but usually in great, numbers. Small gas-cysts containing bacilli were occasionally seen. The necrotic areas bore no special relation to the central veins, the portal veins or the bile-ducts. The latter were normal. The liver tissue in general was well preserved and stained well with the usual dyes.

Spleen.—The spleen showed marked congestion, but no areas of cell destruction and no gas-cysts.

Kidneys.—The kidneys showed cloudy swelling of the epithelium of the convoluted tubules, congestion of the glomerular and intralobular capillaries, and of the veins. No bacilli and no gas cavities were found. The heart showed nothing of interest.

The bacilli noted in the sections of the various organs were identical. They were most numerous in the brain abscesses and in the meningeal exudation. The bacilli varied considerably in size. They were sometimes two μ long, but the most common forms were from four to six μ in length. A few bacilli were seven μ long. Some of the bacilli had square ends, but usually the ends were rounded. They often occurred in pairs, threes and fours, end to end. Not infrequently they were bent or curved, and some were wavy in outline. The bacilli stained well and uniformly with hæmatoxylin, thionin, methylene-blue and by Weigert's method. The last method gave the most clear-cut pictures. With this stain the outlines of the bacilli were often somewhat irregular, due to irregular swelling or contraction of their protoplasm. Slightly clubbed forms were sometimes seen. No stained capsules

were found in the tissues, but occasionally ill-defined masses resembling empty capsules were seen. Careful search of the affected tissues failed to disclose the presence of any other bacteria.

In this case it is evident that the tissue necrosis, the inflammatory lesions and the gas-cysts were due to infection by the bacillus aerogenes capsulatus. The pyogenic properties of this bacillus are now well known.

In my opinion the presence of the bacilli in such great numbers in the nervous system and their relative paucity in the blood-vessels and other organs precludes the idea that they were post-mortem invaders. When an unusual organism is found in association with inflammatory lesions it is no longer thought necessary to assume that the pyogenic cocci have caused the lesions and died out before the case came to bacteriological examination, thus reducing an organism found in large numbers and in pure culture to the level of an accidental and innocuous invader. The complete revolution of our views concerning the pyogenic properties of the typhoid bacillus is an illustration in point. The formation of gas-cysts in the brain, the cerebro-spinal exudation, and in the liver is probably to be regarded as a post-mortem change. The perineal wound must be regarded as the portal of entry for the bacilli. A search of the literature fails to disclose a case of abscess of the brain with cerebro-spinal meningitis due to the bacillus aerogenes capsulatus. I have found this bacillus in the blood-vessels of the brain in several cases without inflammatory lesions. Through the courtesy of Dr. Reuling, I have examined a section through a gas-cyst of the brain of the case he reports in this number of the Bulletin. In every respect it agrees in appearance with gas-cysts of the internal capsule and lenticular nucleus of my case.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Resistance to Quinine of Certain Forms of Malaria.—Dr. Camac.

The value of the following temperature records is both diagnostic and therapeutic. Where the aid of the microscope is not to be had the temperature chart may be all the physician has to guide him in both diagnosis and treatment. It is with the object of drawing conclusion on these two heads that the present malarial temperature charts are exhibited. In each of the following cases the malarial parasite was, of course, found and its type determined, so that the conclusions are reliable as referring to malaria only.

Case I.—J. B. Type Æstivo-Autumnal. *Blood Examination by Dr. Hamburger.* Sept. 30 (day of admission), intracellular hyaline amœboid ring-shaped bodies; one crescent. Oct. 1, a crescent; organisms scarce; hyaline intracellular body. Oct. 2, 10 a. m., quinine gr. x; 12 m., quinine gr. v q, 4h.; p. m., one intracellular hyaline body. Oct. 3, No organisms.

Temperature.—Daily paroxysm; *not reaching normal* during the intervals; temp. normal on Oct. 4.

Treatment.—70 grains of quinine required to control fever. Time required, 3 days.

Case II.—R. B. (colored). Type Æstivo-Autumnal. *Blood examination by Dr. Pancoast.* Sept. 24 (day of admission), 7 p. m., one ring-shaped body. Sept. 25, 10 a. m., ring-shaped amœboid body. 12 m. quin. gr. x; 4 p. m., quin. gr. v. q. 4 h.

Temperature.—Daily parox.; slight drops, *not reaching the normal* (Widal's agglutination negative); temp. normal 27th.

Treatment.—95 grs. required to control fever—3 days.

Case III.—M. J. Type Æstivo-Autumnal? *Blood examination by Dr. Pancoast.* Sept. 27 (day of admission), one ring-shaped body; 10 p. m., quinine gr. x; 12 m., quinine gr. vq. 4 h.

Temperature.—Daily paroxysms; *not reaching normal during intervals.* 2 p. m., 27th, temp. 104.2; fever apparently controlled by quin.; parox. only delayed. 10 p. m., 29th, temp. 101.8. 10 p. m., 30th, temp. normal.

Treatment.—105 grs. required to control fever; time required, 3 days. Especially instructive case as blood examination was not conclusive.

Case IV.—P. C. Type Double Tertian. *Blood examination by Dr. Hunner.* Numerous organisms. 2 sets, 1st full grown in very pale corps; fine, actively motile pigment; 2d, half-grown intracellular pigment, motile; corps somewhat enlarged.

Temperature.—Parox. 27th, from 2 p. m. to 3 p. m. Parox. 28th, 2 p. m. Quin. gr. xx, 2 p. m.; quin. gr. v, 6 p. m. q. 4 h.

Treatment.—50 grains controlled fever, inclusive of time when parox. should have occurred. Time required, ½ day.

Case V.—J. S. Type Double Tertian. *Blood examination by Dr. Hunner.* Two sets of organisms: 1st group, Sept. 13, parox. 2 p. m.; 2d group, Sept. 14, parox. 6 p. m.; 1st group, Sept. 15, parox. 2 p. m.; 2d group, Sept. 16, parox. 4 p. m.

Treatment.—Sept. 16, 4 p. m., subcutaneous inject. quin. gr. xviii. Sept. 17, parox. of 1st set delayed to 6 p. m.; also modified Sept. 15, 104.8; Sept. 17, 102.6. Sept. 17, 6 p. m., intravenous inject. gr. vii ss. Sept. 17, abortive rise at 10 p. m. Sept. 18, fever controlled. Fever controlled by 25½ grs. Time required, 2 days.

Case VI.—J. B. Type Double Quartan. *Blood examination by Dr. Cushing.* Two sets of quartan parasites. Case developed on surgical side. Further blood examination made by Dr. Thayer. Oct. 26, 10 p. m., paroxysms complete; quin. grs. v, 2 and 4 p. m. Oct. 28, 2 a. m., paroxysms complete. Oct. 29, 12 noon, quin. grs. v q. 4h. Oct. 30, slight parox. Oct. 31, slight parox.

Treatment.—30 grs. greatly modified parox. of two group; 75 grs. controlled fever.

There are to be observed in these six cases several striking features: 1st, The marked resistance to quinine of the æstivo-autumnal type. 2d, The tendency of the æstivo-autumnal not to reach normal during the intervals. 3d, No form resisting the quinine beyond 3 days.

The most effectual time to exhibit quinine has been fully investigated by Golgi; Marchiafava and Bignami, and Case VI of the present series demonstrates well Golgi's observations. He finds that quinine administered in quartan fever, 4 or 5 hours (even in small doses) before segmentation readily kills the young forms, but has no influence upon the adult forms, the following paroxysms occurring uninterruptedly. The tertian, however, is readily influenced by the administration of quinine just before the paroxysms (Case IV), the following paroxysms being prevented or delayed. From the teachings of Marchiafava and Bignami the following may be concluded for tertian and quartan fever:

Full dose at crisis:
1. Parox. prevented.
2. Aborted.
3. Delayed 6-24 hours.

Full dose 6 hours before crisis:
1. Delayed.
2. Aborted.
3. Pseudocrisis.

By watching the chart and observing first its character uninfluenced by quinine, then its character after the administration of quinine, and noting at the same time when the quinine was administered with reference to the paroxysm, the diagnosis not only of malaria but of its type may sometimes be made. Fever which shows no signs of breaking three days after the administration of full doses of quinine every four hours is other than malaria; if it yields earlier than the third day, on moderate doses, it is likely to be of the tertian or quartan type, whether double or single. The tendency of the æstivo-autumnal fever to resist quinine has led the Italian observers to speak of the gradual destruction of the parasite as one of "fractional sterilization," and this tendency would induce the careful physician to prolong his quinine for a greater period in dealing with this form. Here, however, we may take as a guide the fact that the æstivo-autumnal fever often fails to touch normal during the intervals between paroxysms, whereas the tertian and quartan more commonly do. To those cases therefore who bear quinine badly it may be discontinued earlier and with greater safety in the tertian and quartan than in the æstivo-autumnal.

It may, however, with profit, be repeated, and repeated emphatically, that fever which does not show signs of *breaking* within three days, when properly met by quinine, is other than malarial, and quinine is being given not only to no advantage, but in many cases with harmful effects.

We have, therefore, in the proper observation of the temperature chart, both a diagnostic and therapeutic guide, though we have not the aid of the microscope.

It may be interesting in this connection to mention a recent conversation with Dr. John T. Metcalfe, one of Louis' students, who remembers the pre-quinine days. I think it was about 1820 that quinine was separated by Pelletier, prior to which Peruvian bark was used exclusively. The preparation known as Peruvian paste was so thick that it could be just swallowed. A tablespoonful was taken at a dose, and frequently vomiting was so severe as to require the use of opium. A 3-ounce bottle of quinine was brought to Natchez, Miss., and was sold for $90.

A New Method of Staining Malarial Parasites.—Dr. Futcher.

As Dr. Lazear and myself, during the past winter, came across a convenient method of staining malarial parasites in dry specimens, I thought it might be of interest to report it to the society. We do not claim originality, either for the method of fixing, or the method of staining, the organisms, but, so far as the combining of the two methods is concerned, we think it has not been done before. It is a very quick process and very serviceable in cases where one is called out to see a suspicious case and has not a microscope at hand with which to examine the fresh blood.

The dried-blood specimens, made in the usual way described by Ehrlich, are then fixed in a ¼ per cent. solution of formalin in 95 per cent. alcohol. It is important that the formalin solution should be made up fresh each time it is used. We have found satisfactory results by adding four or five drops of a ten per cent. aqueous solution of formalin to 10 cc. of 95 per cent. alcohol just before using. This method was first described by Benario in the Deutsche Medicinische Wochenschr., No. 27, 1894. He used a 1 per cent. solution of formalin in 90 per cent. alcohol, however. He stated that not only was the hæmoglobin of the red cells well preserved, but the granules and nuclei of the leucocytes were well fixed and took the stain particularly well. The cells were especially well stained with eosin and hæmatoxylin. The specimens are fixed in this solution for only one minute, washed in water, blotted and then stained in the special mixture.

As to the staining agent, our attention was first drawn to the use of thionin by Dr. W. G. McCallum, who referred us to an article by E. Marchoux, in the Annales de l'Institut Pasteur, Vol. ii, p. 640, 1897, in which the author gives a report on the malarial fevers of Senegal, and in which he describes his method of using thionin in staining the parasites. The author considered it especially serviceable for staining malarial organisms, but instead of formalin he used the ordinary alcohol and ether fixing method and, so far as we know, the use of formalin and this stain have not been combined before. He makes a saturated solution of thionin in 50 per cent. alcohol, of which 20 cc. are added to 100 cc. of a 2 per cent. carbolic acid solution. This solution can be kept in stock and used as required. It is perhaps better to keep the stain for some time before using as it improves with age. Thionin phenate is formed, which is believed to be the active staining agent. Only 10 to 15 seconds are required for staining.

The malarial parasites come out very distinctly as reddish-violet bodies with this stain, and it is especially serviceable in staining the ring-shaped bodies of the æstivo-autumnal infection. These are very hard to distinguish in fresh specimens and usually do not stain satisfactorily with eosin and methylene-blue. Any one who has stained specimens in this way knows how he has regretted, on examining them two or three months later, to find that they have faded. With the thionin stain the parasites retain the color much better than they do when stained with methylene-blue.

The method of fixing and staining malarial parasites is then as follows:

Make the ordinary smear preparation, fix in the formalin solution for one minute, wash in water, thoroughly dry, stain with the thionin solution for from ten to fifteen seconds; ten will probably give the most satisfactory results. Wash off the excess of stain, blot, mount in balsam and the specimen is ready to be examined. The whole operation does not last more than two minutes from the time you begin to fix until it is ready for examination, whereas with the old method of fixing with alcohol and ether, one usually has to wait two hours to get satisfactory results, and even then it is often found, if eosin and methylene-blue have been used, that the hæmoglobin of the red cells has not been properly fixed and the cells show peculiar vacuolic areas. With the formalin fixing and thionin staining the protoplasm of the reds is well fixed and practically unstained, and the parasites stand out

distinctly as reddish-violet bodies in the substance of the red cell. The ring-shaped bodies of the æstivo-autumnal variety come out much better than with any other agent in use.

We also used the thionin stain to try and bring out the flagellated processes in the æstivo-autumnal infection. Probably one of the most convenient methods for obtaining permanent preparations of the flagella is that described by Sakharov, in which an ordinary specimen on the slide is made and at the same time several specimens of blood are taken on coverslips, leaving the latter in contact with each other in a moist chamber and watching the ordinary preparation under the microscope until flagellation begins, when the coverslips in the moist chamber are taken out and drawn apart and dried. One will then most likely catch the organisms in the flagellating stage. We have fixed some of these by heat and then stained with thionin, and have obtained some good specimens showing the flagellate processes coming off from the body of the parasite. At this time we had not been using the formalin fixing, but there is no reason why it should not be substituted for the heat.

This method of fixing and staining is not to supersede the examination of the specimen of fresh blood, always the most satisfactory method, but only where staining is the only resource and rapid results are desired. We have placed under the microscope on the table specimens of the three types of malarial organism stained by this method.

Dr. Flexner.—There is a method, you will remember, which was worked out by Dr. Mallory for staining the amœba coli. The specimen is stained in thionin and placed in a weak solution of oxalic acid to remove the coloring matter from all other cells except the amœbæ. I also had the opportunity of studying recently some specimens of amœbic dysentery stained by Dr. Harris of Philadelphia, with toluidin blue and the organisms are as easily made out as when stained with thionin. I do not know whether these methods would succeed with the malarial parasite, but they might be tried.

Dr. Lazear.—During the summer I tried the toluidin blue for the malarial parasite. It is fully as good as methylene-blue, but does not stain so deeply as the thionin.

Dr. Thayer.—It appears to me that the method of staining advised by Dr. Futcher is one which is of very considerable practical value. It is often impossible for the busy practitioner to examine the fresh specimen of blood, and most of the other methods of preparation are rather delicate proceedings, at least if one wishes to obtain really good specimens. A thoroughly satisfactory method which can be carried out almost inside of two minutes is a great advance.

I should like to emphasize particularly its value in staining the æstivo-autumnal parasites. The hyaline bodies take up all dyes very feebly, and it is often extremely difficult for the unskilled eye to distinguish them. By Dr. Futcher's method of staining with thionin, however, a perfectly satisfactory specimen may instantly be obtained. I know of no method which brings out the æstivo-autumnal parasite so well.

Laparotomy for Intestinal Perforation in Typhoid Fever.—[See Bulletin for November Discussion, 1898.]

Dr. Thayer.—I had the good fortune to observe the first case which Dr. Cushing has mentioned throughout the greater part of its course. I happened to walk into the ward on the night upon which the second operation was done and found the boy in a condition of profound collapse. This had come on very suddenly, Dr. Cushing having seen the child but a short time before. When I saw him he had been vomiting; the skin was cool; there was profuse sweating; the temperature had fallen several degrees; there was abdominal tenderness; the pulse was feeble and rapid; the face was drawn; the cheeks and eyes sunken. There could scarcely have been a more typical picture of acute peritonitis. And yet, when the abdomen was opened, there was not only no peritonitis, but there was not enough disturbance to suggest the existence of obstruction to any one present. Such a picture is an excellent demonstration of the difficulties which may stand in the way of a correct diagnosis in these cases.

What Dr. Cushing has said of the leucocytes is, it seems to me, of considerable importance. I have no doubt that it is quite true that in an individual with distinct evidences of perforative peritonitis a normal or subnormal number of leucocytes is a very bad prognostic sign. I remember one or two instances of general streptococcus septicæmia where the leucocytes were normal or subnormal in number; one case in particular where there were but 3000 leucocytes to the cubic millimeter. As long ago as 1892, Werigo showed that after inoculating animals with cultures of pyogenic bacteria there occurs primarily a reduction in the number of leucocytes to the cubic millimeter. In the milder cases this initial fall is followed by a subsequent leucocytosis. In the particularly malignant and rapidly fatal cases, however, no subsequent rise in the number of leucocytes occurs. The same condition has been noted experimentally by various other observers. And I am inclined to believe that, as in pneumonia, so in other malignant general infections, a subnormal number of leucocytes may be regarded as a bad symptom, and it is not at all impossible that in Case III the fall in the number of leucocytes following the direct evidence of perforation may well have been associated with the sudden onset of what proved to be a rapidly fatal streptococcic infection, the previous leucocytosis having been due to the moderate local peritonitis about deep ulcers.

Monday, December 19, 1898.

Presentation of Pathological Specimens.—Drs. MacCallum and Harris.

Dr. MacCallum presented a case exhibiting multiple metastases from a sarcoma primary in the pelvis. The patient was a young man, aged 21, who had complained of chills and obstinate constipation with great pain on defecation. There was also severe pain in knee, hip and back, and recently considerable loss in weight and strength. Physical examination revealed signs of consolidation at left apex; tumor masses projecting laterally out of the pelvis in the inguinal regions; and per rectum a large smooth mass filling the pelvis over which the mucosa of the rectum could be

moved. There were also several subcutaneous nodules. After a very painful illness the patient developed a pleurisy and died without any great elevation of temperature.

At the autopsy the most extensive tumor growth was found in the pelvis. The pelvis was completely choked by the new growth which projected over its brim and formed the nodules palpated during life. The mass lay between the bladder and intestine, projecting into the bladder and forming a large ridge across its posterior wall. The prostate retained almost its normal appearance, the median lobe being apparently unchanged. Rectal mucosa was not involved. This large tumor was directly continuous with the chain of retroperitoneal glands which were densely matted together and surrounded the recto-vesical cul-de-sac. Sections showed that the tumor—an alveolar large round-cell sarcoma with giant cells—had invaded the bladder from without, as remains of epithelium exist over the intra-vesical projection. The prostate was almost completely replaced by the tumor mass, and the seminal vesicles pushed far back towards the rectum. Metastases occurred in the testes, liver, epicardium, lungs and mesentery, as well as the subcutaneous tissues. The lymphatic glands, with the exception of the immediately adjacent retroperitoneal glands, were very slightly involved.

In the lung, in addition to a mass at the hilum, the metastases were chiefly in the form of flat, button-like nodules on the pleural surface, and on cutting up the arteries which run to these nodules, the arterial walls were seen to be infiltrated with tumor cells so as to form a thick cord-like structure with relatively narrow lumen—a few of these arteries were actually plugged with masses of tumor cells, evidently indicating the channel of metastasis. The possibility, perhaps, cannot be excluded that the perivascular involvements in the neighborhood of the subpleural nodules are merely extensions in the lymphatics of the vessels from the tumor masses which themselves may have arisen from an infection of the pleura—an idea supported by the extensive involvement of the costal pleura.

The very similar cases of Andree and Zenker (both reported in Virchow's Archiv) were referred to.

Dr. Harris.—The greater interest of this case, no doubt, lies in the pathological statement that Dr. MacCallum has presented, but the bacteriological findings will, I think, prove by no means unworthy of consideration.

The bacteriological analysis of the autopsy was as follows: The streptococcus pyogenes was isolated in pure culture from the liver, the spleen and a sarcomatous nodule on the abdominal wall; associated with this organism was the bacillus proteus vulgaris in a culture obtained from the lung.

Subsequently, additional interest was added to the case by the accidental infection with the streptococcus of Dr. Cushing and Miss Reed. In the former, the symptoms of beginning trouble appeared within six hours at the site of a small prick in one finger; within twelve hours the axillary glands and lymphatics of the limb were swollen and tender. The symptoms of infection becoming more pronounced, surgical aid was required, and, with excision of the infected area, recovery soon set in. From the excised portion of the finger the streptococcus pyogenes was obtained in pure culture.

In the latter case of infection the trouble was entirely local in character, being confined to the tissues at the root of a finger-nail. Redness, pain, swelling and pus formation were the cardinal symptoms. The finger received surgical treatment and slowly healed by granulation. Coverslips from pus showed streptococcus. In consideration of these two cases of accidental infection it was thought advisable to continue the bacteriological study of the organism, and tests were made to determine its virulency upon mice. The first mouse received subcutaneously 0.3 cc. of a bouillon culture. It was found dead next morning, and had probably died within twelve hours—rather a rapid result. The animal was autopsied, but all that was found was a subcutaneous œdema with possibly a small focus of necrosis. The inguinal glands were swollen, but not hemorrhagic. The axillary glands were in the same condition, and all the vessels leading to them were tremendously engorged. The lumbar and mesenteric glands were increased in size. The spleen was greatly swollen, dark-red and soft; the liver was also enlarged and friable; the kidneys in the same state, but pale instead of dark. Cultures from the organs of the mouse were negative, the organism being recovered only from the site of inoculation.

From that organism the second mouse was inoculated, using only one small loopful from the agar culture and administered beneath the skin. This mouse died in sixty-five hours, and the same appearances were found on autopsy of this animal. In addition the lungs showed numerous broncho-pneumonic patches. From these and from the heart's blood the organism was obtained in abundance.

From a liver culture of this mouse a third mouse was given the same quantity, and it died in less than sixty hours.

Upon the grounds of susceptibility to infection with the streptococcus pyogenes we are at once struck by the fact that the human being is very much more prone to this infection than mice, for, in a large number of cases occurring in the human subject, the isolated organism fails to kill a mouse inoculated with it. I can call to mind several occasions where I injected rabbits and mice with streptococcus obtained from cases of puerperal septicæmia, and had entirely negative results. Therefore, upon the high degree of virulence exhibited by this streptococcus, is the bacteriological side of the case presented.

NOTES ON NEW BOOKS.

Twenty-ninth Annual Report of the Massachusetts State Board of Health. (*Boston: Wright & Potter Printing Co.*, 1898.)

The Massachusetts State Board of Health Report for 1897 contains the records of work done by the Board during the year set forth in the lucid style so long characteristic of preceding issues. A general report, including a joint report upon the restoration of Green Harbor, is followed by a section relating to water-supply and sewerage. This section contains a report to the legislature, advice to cities and towns regarding their respective water-supplies and sewerage systems, records of chemical and microscopical work done in the examination of water-supplies and rivers, water-supply statistics and a complete account of the work at the Lawrence Experiment Station on sewage purification and the filtration of

water. The sewage purification of cities and towns in Massachusetts is finally discussed.

Section 3 consists of a report on food and drug inspection and the analytical examination for adulterations, etc.

Sections 4, 5, 6 and 7 describe the work and results of the State Bacteriological Laboratory, including diagnostic examinations and the making of antitoxin.

Statistical summaries of disease and mortality follow, and a review of the sanitary statistics of the various towns of the commonwealth completes the report.

There is, perhaps, no publication in this country in which statistics are more carefully worked out, or made to yield more definite information, than those collected by the Massachusetts State Board of Health, largely due to the fact that its well-known secretary is one of the most careful and patient statisticians in this country.

From this report, we gather that infectious diseases in Massachusetts have steadily decreased during the last forty years, with the exception of a slight rise in 1896. An outbreak of small-pox, limited to about eighteen cases, occurred in Boston and neighboring municipalities during the first half of the year. In this connection, and in view of the recent retrograde changes in the vaccination laws of England, it is interesting to note that during the ten years (1888–1897) the death-rate in Massachusetts amongst vaccinated small-pox patients was 6.3 per cent., and amongst unvaccinated small-pox patients 25.5 per cent., about four times greater. We may note here that in Massachusetts, also, the vaccination laws suffered, in 1894, an unnecessary amendment, still in force, allowing any regular physician to certify to the unfitness of a child for vaccination, so exempting the child from the legal restrictions otherwise imposed. The granting of such exemptions should certainly be left to the discretion of boards of health.

Typhoid fever showed a reduction of about twelve per cent. Careful consideration of the mortality lists of the different Massachusetts towns confirms once more the rule that a continued high death-rate from this disease in any one community points to the probable pollution of the water-supply of that community and calls for careful investigation. The number of diphtheria cases steadily decreased during the years 1894, 1895 and 1896. The fatality of cases diminished in a much greater ratio due probably to improved treatment and greater sanitary precautions. It can be definitely established that the fatality of epidemics, as well as their extent, is generally lessened by rigid supervision and painstaking care.

The epidemic of cerebro-spinal meningitis, which occurred early in this year (1897), has been exhaustively treated in the monograph of Councilman, Mallory and Wright, to whom the investigation of the epidemic was entrusted by the State Board of Health. This monograph is abstracted in the report. It is interesting to compare with this epidemic of the year 1897 in Boston, the similar epidemic in Chicago during the year 1898, an account of which has been recently issued by the Chicago Health Department.

The food and drug inspection and examination upset some of the popular notions regarding the supposed extensive adulteration of foods. The adulterations in most cases are usually of a nature commercially fraudulent rather than physiologically harmful. It is curious to note that the production of pure butter is provided for by the maintenance of no less than four separate sets of officials, while on the other hand, the laws supposed to control the sale of poisons allow the unlimited sale of proprietary medicines containing violent irritating poisons or narcotics, a defect certainly requiring correction.

In most of the large cities of the State, bacteriological laboratories have been established for the diagnosis of diphtheria, tuberculosis, malaria, etc. The bacteriological laboratory of the State Board, in addition to the production of diphtheria and tetanus antitoxin, undertakes diagnostic work for those communities unprovided with a local laboratory. The use of formaldehyde as a gaseous disinfectant has become quite general throughout the State.

A large part of the report deals, as usual, with the analysis of the public water-supplies of the State, and also of rivers not now used for water-supply but receiving sewage from communities on their banks, a very provident proceeding; also with the investigations of the Lawrence Experiment Station on the filtration of water and disposal of sewage. In January, 1897, the laboratory for water analysis was transferred from the rooms of the Institute of Technology to the State House. Both this laboratory and that of the Experiment Station at Lawrence are now under the charge of Mr. H. W. Clarke. The chemical and microscopical methods developed in these laboratories continue in use. The bacteriological work is restricted to the usual efficiency tests of the filters and examination of Merrimac river water at the Experiment Station. No record of bacteriological work on the other public water-supplies is given. Owing to the distance which many of the samples of water must travel to reach the laboratory, and to the difficulty and expense of providing cold storage in transit for them, we think it probable that the additional information which may be obtained by bacteriological analysis of the water-supplies of the whole State is likely always to be restricted to qualitative work, omitting the quantitative as impracticable. Nevertheless, so many interesting and valuable chemical and biological determinations embracing not only the mere analytical results, but also the methods of analysis themselves, have come from the laboratories of the State Board in the past, that one is tempted to hope the near future may see quantitative bacteriological methods employed, for a time at least, on all the water-supplies of Massachusetts, if only to demonstrate their practicability or impracticability, in such work as the Board undertakes for the public. We think that the value of such bacteriological work is considerable and its practicability has been already amply demonstrated, certainly where the laboratory can be reached within a few hours of the collection of samples. The Lawrence experiments this year (1897) have been devoted to a continuation of the experiments of last year (1896) on the purification of tannery, paper-mill and wool-scouring establishments, on the filtration of highly polluted waters, and on the removal of iron from the waters of certain parts of the State.

Under food and drug inspection, and in addition to the ordinary routine work, the foil used for wrapping various preparations, the metal stoppers of liquid preparations, etc., have been examined for lead with interesting results. In certain countries, the inspections of these wrappers and stoppers as well as of culinary utensils, beer faucets, etc., is controlled by law. The refractometer, principally, is used in the detection of adulteration of such fats as butter, lard, olive oil, etc. A large percentage of cheap jellies were found to contain no trace of the raspberry, strawberry, etc., which the label proclaimed as present.

The report of the bacteriological laboratory of the Board at the Bussey Institute, under the charge of Dr. Theobald Smith, contains a number of tables illustrative of the results of the use of antitoxin, classification of the bacteriological diagnoses made and of the examinations for the malarial organisms.

Under the *Health of Towns*, an epitome of the reports of the various boards of health of the State is given. The action of the Lowell authorities in attaching a "poison" label to all the faucets in the mill fed with canal water shows that they at least are troubled with few doubts on the dangers of polluted water-supplies.

In conclusion, we may congratulate the State Board of Health, through its president, Dr. Walcott, on the continued excellence of its Annual Report as exemplified in this issue. It must be confessed that we miss the detailed accounts of methods of water analysis, their applications and limitations, which have made certain of the previous reports indispensable adjuncts to chemical, biological and bacteriological laboratories throughout this country. No one institution has contributed more to these subjects in the past; certainly no one of these subjects is yet exhausted. We believe that much of the information bearing on these points is still practically unknown in many sections of the country. Nor can we do other-

wise than regret that the able pen of Dr. Smith has not yielded to this report some account of the routine methods in his department. Changes in technique, however slight, are often of considerable value, and in any case, the repeated publication of even an unchanging routine, wearisome as it may seem, gradually tends to bring about a greater uniformity in method as new laboratories are established and the latest and most successful methods are considered for adoption. To the sanitarian and statistician, in general, the present volume will prove fully as interesting as its predecessors, but the student, the analyst and the ubiquitous "laboratory man" will certainly turn back, with some disappointment, to the reports of 90-96.

To the general public, the explanations accompanying some of the statistical tables of this report and the brief summaries of the conclusions to be deduced from the tables are most valuable. We can only wish that this method of making clear to "the laity" the meaning of the endless succession of figures in which statisticians delight was more extended in this report and more generally followed in others of a similar nature. H. W. H.

A Primer of Psychology and Mental Disease. For use in Training Schools for Attendants and Nurses, and for Medical Classes. By C. B. Burr, M. D., Medical Director of Oak Grove Hospital, &c. Second Edition. Thoroughly Revised. (*The F. A. Davis Co., Philadelphia, New York, Chicago*, 1898.)

The appearance of a second edition of Dr. Burr's Primer of Psychology is, in itself, evidence that it has met a want and, considering that there are other more or less similar works to compete with it in its rather limited circle of patronage, is an indication of its worth. The present edition, in addition to the general revision, has had added an address given before the Training School class of the Eastern Michigan Asylum, in 1895, a valedictory address on the occasion of his leaving that institution.

If one is to offer any criticism of the work it would be on some minor point, such, as for example, the statement that in mania there is no tendency to suicide. Maniacs do sometimes commit impulsive suicide, and like most other insane are to be considered as rather uncertain in their conduct and needing watching. This and possibly one or two other similar statements should be less absolute, and in a future edition their modification is suggested. As a treatise for the instruction of hospital attendants we can heartily recommend this book.

Archives of the Roentgen Ray. Edited by W. S. Hedley, M. D., and Sidney Rowland, M. A. Vol. II, No. 4; Vol. III, No. 1. (*W. B. Saunders, Philadelphia*, 1898.)

These two issues of this now well-known publication appear to be fully equal to their predecessors, and to contain the usual number of scientific communications. Most of them are of a rather technical character, relating to the physical characteristics of the X-Rays and their management, as would be naturally expected, but one or two are of medical interest. One of these is the preliminary notes of Drs. Wolfenden and Ross on the influence of the Roentgen Rays upon the growth and activity of bacteria and micro-organisms, in which they were found to have a very marked stimulating influence on the bacillus prodigiosus. The authors are continuing their research on the pathogenic bacilli especially, and it will be an important gain if they can give us some authoritative data on their behavior under the action of the rays.

The same issue reproduces from the *British Medical Journal* an abstract of the papers and discussions on the uses of the Roentgen Rays in the diagnosis of tuberculosis at the late congress on this disease at Paris last summer. Their value, in this particular direction, seems fairly settled, or at least highly probable, when they are utilized by experienced operators.

On Cardiac Failure and its Treatment. With special reference to the use of baths and exercises. By Alexander Morison, M. D., Edin., M. R. C. P., Ed. (*London: The Rebman Publishing Co., Ltd.*, 1897).

This work is a scientific monograph on cardiac weakness, a condition that is sometimes too little recognized, though, unfortunately frequent enough and often of serious importance, even without actual irreparable organic disease affecting the mechanical action of the heart. Whether it be the nervous system that is at fault, or the muscular tissue has lost its tone, or the heart is embarrassed by the mal-coöperation of other important organs or tissues, the general result is alike in all, a cardiac failure, varying only in degree in any particular case. The recognition and treatment of each and all of these factors is an important question, and serves to indicate how complete in this, as in other affections, the investigation of the disorder should be from the very beginning of the treatment.

The book appears to give within its compass reliable and thorough monographs of its subject, and the latter portion on the treatment of these conditions will be doubtless found valuable and suggestive. The remarks upon and descriptions of the gymnastic and hydrotherapeutic methods ought to be particularly useful as comparatively new in our literature, and the author has supplemented his own skilled observations and opinions with an appendix by Dr. Groedel, of Bad-Nauheim, who has also had the revision of the chapters on these special subjects.

BOOKS RECEIVED.

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Annual and Analytical Cyclopædia of Practical Medicine. By Charles E. de M. Sajous, M. D., and one hundred associate editors, etc. Volume II, 1899. 4to, 607 pages. The F. A. Davis Co., Publishers, Philadelphia, New York and Chicago.

The American Year-book of Medicine and Surgery. Collected and arranged with critical editorial comments by S. W. Abbott, M. D., J. J. Abel, M. D., *et al.* Under the general editorial charge of George M. Gould, M. D. 1899. 4to, 1102 pages. W. B. Saunders, Philadelphia.

Saint Thomas' Hospital Reports. New series. Edited by Dr. Hector Mackenzie and Mr. G. H. Makins. Vol. XXVI. 1898. 490 and 170 pages. J. & A. Churchill, London.

3000 *Questions on Medical Subjects Arranged for Self-Examination.* Second edition. 32°. 1899. 189 pages. P. Blakiston's Son & Co., Philadelphia.

An American Text-book on Diseases of the Eye, Ear, Nose and Throat. Edited by G. E. de Schweinitz, A. M., M. D., and B. Alex. Randall, M. A., M. D., Ph. D. 1899. 4to, 1251 pages. W. B. Saunders, Philadelphia.

Saint Bartholomew's Hospital Reports. Edited by N. Moore, M. D., and D'Arcy Power, F. R. C. S. Vol. 34. 1899. 8vo, 396 and 258 pages. Smith, Elder & Co., London.

Thirty-fourth Annual Report of the Trustees of the Boston City Hospital, with report of the Superintendent, February 1, 1897, *to January* 31, 1898, *inclusive.* 1898. 8vo, 215 pages. Municipal Printing Office, Boston.

Transactions of the Medical Society of the State of North Carolina, Forty-fifth annual meeting held at Charlotte, N. C., May 3, 4 and 5, 1898. 8vo., 173 and 50 pages. Carolina Publishing Co., Winston, N. C.

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ACUTE DIFFUSE GONOCOCCUS PERITONITIS.

By Harvey W. Cushing, M. D.

(*From the Surgical Clinic of Dr. Halsted, The Johns Hopkins Hospital.*)

Owing to the influence of Bumm's original assertion, that gonorrhœal processes remain limited to surfaces lined by mucous membrane, it had until comparatively recent times, been generally doubted that the gonococcus of Neisser, without the association of the more common pyogenic organisms, was capable of inducing an acute general peritonitis. It is however, now recognized that structures other than those of an epithelial character are liable to invasion by the gonococcus and, indeed, parts covered by endothelium seem particularly liable to attack by this organism. Thus the joints, plura, peri- and endocardium are liable to gonococcal infection, and although these affections are metastatic in character, and occur during the course of a general gonococcus septicæmia, they nevertheless suffice to prove the untenableness of Bumm's original statement. Nevertheless surgeons have clung to the belief in the immunity of the peritoneum to gonococcal infection, and it has generally been granted that gonorrhœal processes in women are checked in the neighborhood of the abdominal ostia of the tubes, where by continuity of extension, a peritonitis otherwise might readily be induced. We must for the present continue to believe that such an inhibition of the growth of the organisms does usually occur when the serosa is reached, but whether under unusual circumstances a general peritonitis may not follow, by implantation of gonococci from the tubes upon the peritoneum, has hitherto been regarded as extremely improbable. The usual conception is concisely expressed in a recent paragraph by Frederick Treves,* as follows:

"Peritonitis has been met with in association with gonorrhœa, but inasmuch as the gonococcus cannot survive in the peritoneal cavity it is doubtful whether peritonitis due to the gonococcus alone has any existence. . . . . It is very probable that a mixed infection is the cause of the pyosalpinx often met with in gonorrhœa. That pyosalpinx may lead to acute peritonitis is undoubted, but it has not been demonstrated that such a complication is due to the action of the gonococcus alone; it is probably the outcome of a mixed infection. . . ."

Even among those few investigators, who have devoted their attention from an experimental as well as a clinical standpoint to the possibility of this complication of gonorrhœa in

* Fred'k Treves, Allbutt's System of Medicine. Vol. III, p. 609, 1897.

women, the subject remains one of debate for the want of one link in the chain of evidence, which it is hoped that this communication will establish.

The recent observation at the Johns Hopkins Hospital of two cases of diffuse peritonitis, due to pure gonococcal infection, which it is the design to report, has led to the following brief historical review of the literature dealing with the question outlined in the preceding paragraph.

Bumm,* in 1889, published the following statement in which the principles laid down by most subsequent writers can be seen reflected. "Ab es eine gonorrhoische Entzündung des Peritoneum giebt ist mir immer sehr Zweifelhaft gewesen. Die Mikroben der Gonorrhöe vermögen nur auf Schleimhäuten pathogene Wirkungen zu entfalten, gehen aber in Serösen Höhlen zu Grunde. Reiner gonorrhöischer Eiter, der sich aus geplatzten Tubensäcken in's Peritoneum ergiesst, wirkt in der Regel nun als aseptischer Fremdkörper. Es wird abgekapselt, etc." He goes on to say that only a mixed gonococcal infection can be followed by a septic peritonitis.

At the meeting of the German Gynæcological Society, held in Bonn, in 1891, Bumm† further emphasized his views. He believed that gonorrhœal infections ran a course as a superficial mucous membrane affection merely and never penetrated the deeper connective tissue in which the gonococcus would perish: that the organism of Neisser had nothing to do with septic processes, which occurred only through the medium of mixed infections: that the gonorrhœal process, usually localized in the urethra and cervix, under certain influences, primarily that of menstruation, but also during the puerperium, and from coition and instrumentation, might extend to the endometrium of the body and tubes. Beyond these parts, however, he believed the process did not pass, being limited by the endothelial peritoneal surface.

At this same meeting Wertheim‡ presented the results of some clinical and experimental investigations which question the assertion as to the immunity of the peritoneum in Bumm's sense, and which remain to-day the most important contribution to this subject.

His observations, which are directly in opposition to those of Bumm, demonstrated conclusively that at all events a *circumscribed* pure gonococcal peritonitis could be produced experimentally in animals and was possible in human beings.

In a carefully conducted series of experiments he found that the inoculation into the abdominal cavity of certain animals of a pure culture of gonococci, which organisms he had cultivated successfully upon human blood-serum agar, would produce a localized peritonitis, provided that there was introduced at the same time a non-absorbable material. For his purposes nutrient agar sufficed. He found, however, that even in white mice and guinea-pigs, the most susceptible of the lower animals, the process remained localized, was evanescent and never fatal. The acute circumscribed seropurulent reaction consisted of a deposit of pus cells and gonococci in great abundance on the hyperæmic serosa of the bowel. Nor was this all, for in sections the gut showed the gonococci penetrating deeply under the serosa and between the muscle bundles in ever-increasing intensity for about seventy-two hours, after which the multiplication of the organisms would cease and they would become more difficult of cultivation. The control animals would invariably recover. In his entire series of laparotomized animals no instance of mixed infection was encountered, and he recovered the introduced organisms in pure culture, and afterwards conclusively demonstrated their nature by the production of a specific anterior urethritis in man.

He further demonstrated that in a considerable percentage of cases of chronic salpingitis, which, from the absence of any growth upon ordinary media had previously been supposed to be sterile, a pure culture of gonococci could be obtained upon his blood-serum agar. Similarly from two cases of ovarian abscess he isolated pure cultures of these organisms.*

By his experimental and pathologic studies, therefore, Wertheim showed that the gonococcus was capable of multiplication upon the peritoneal serosa and in the tissues, and of inducing an acute localized, though evanescent, peritonitis. Similar occurrences in the human peritoneum and the possibility of a diffuse peritonitis of similar nature remained undemonstrated.

Wertheim† in a subsequent report published a case in which, during a laparotomy for salpingitis, he found an extensive acute pelvic peritonitis. In the exudate he demonstrated gonococci and succeeded in cultivating them on his blood-serum agar. The abdominal ends of the tubes were open and discharging pus. The fimbriæ were free from adhesions. Had the process been left to itself it would have gone on to organization of the exudate and the formation of extensive pelvic adhesions, the usual sequel of these conditions. The author believes this to be the first assured case of acute gonococcal infection of the peritoneum in a human being.

Since Wertheim's communications occasional contributions

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* Bumm, E. Zur Aetiologie der septischen Peritonitis. Münchener med. Wochenschr., Bd. XXXVI, No. 42, p. 715, 1889.

† Bumm. Ueber die Bedeutung der gonorrhoischen Infection für die Entstehung schwerer Genitalaffectionen bei der Frau. Verhandlungen der deutschen Gesellschaft für Gynäkologie, IV. Kongress, 1891, p., 359.

Ref. Centralbl. f. Gynäkologie, Bd. XV, p. 448, 1891. Ref. Journal of Obstetrics, Vol. XXIV, p. 1265, Nov., 1891.

‡ Wertheim, Ernest. Zur Lehre von der Gonorrhoe. Verhandlungen der deutschen Gesellschaft für Gynäkologie, IV. Kongress, 1891, p. 346.

Die ascendirende Gonorrhoe beim Weibe. Bakteriologische und klinische studien zur Biologie des Gonococcus Neisser. Archiv für Gynäkologie, Bd. XLII, p. 1, 1892.

Ref. Journal of Obstetrics, Vol. XXIV, p. 1379, Nov., 1891.

Ref. Centralbl. f. Bakteriologie, Bd. XII, p. 105, 1892.

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* The frequent demonstration by other observers since Wertheim, of gonococci in the pus of ovarian abscesses, when the organisms are no longer demonstrable in the chronic peritonitis about the appendages, is most naturally explained on the supposition that the bloodclot of a ruptured follicle offers a more favorable culture medium for their maintenance than does the peritoneal serosa.

† Wertheim, Ernest. Ein Beitrag zur Lehre von der Gonokokkenperitonitis. Centralblatt für Gynäkologie, Bd. XVI, p. 385, 1892.

Ref. Centralbl, f. Bakteriol. und Parasiten, Bd. XII, p. 108, 1892.

to the subject have been made by various writers, all of rather negative value.

Menge,* at the Tenth International Congress in Berlin in 1891, reported the results of examination of twenty-six cases of purulent salpingitis. He found micro-organisms on eight occasions and gonococci on three, but, like Bumm, he failed to demonstrate the latter in inflammatory processes of the peritoneum. Menge, however, unlike Bumm, does not commit himself, but leaves the problem unsolved as to whether the acute and chronic pelvic peritonitides, which we find accompanying purulent gonorrhœal salpingitis, are due to a specific gonococcal infection, or to the chemical irritation of the overflowing secretion, or are the product of a definite mixed infection.

Zweifel,† in his discussion of Menge's paper, gave the conclusions drawn from a great number of personal observations, namely, that the formerly denied sequence of infection of the abdominal cavity with gonococci stood in contradiction to clinical experience. He believed in the existence of a gonococcal peritonitis, and that the organisms can be found only in the very acute cases, such as, for example, do not last longer than a week. He acknowledged, however, that definite proof to support this statement had not yet been brought forward.

Similarly Charrier,‡ in Pozzi's clinic was not able to cite a definite instance of such acute gonococcal peritoneal inflammation, although he believed in its existence. He considers it a short-lived process and one complicated, as a rule, by concomitant infection with other pyogenic cocci.

Menge reported a case to the Gesellschaft für Geburtshülfe in Leipzig, in 1893,§ in which, following the correction, under anæsthesia, of a retroflexed uterus associated with a small pyosalpinx, a general peritonitis supervened. Zweifel operated and found a double pyosalpinx with beginning general peritonitis. The pus from the tubes showed a few gonococci on culture. None, however, could be demonstrated on cover-slip preparations. The abdominal contents were negative culturally, nor could any organisms be found on stained preparations. The patient recovered and Menge believed that the peritonitis was attributable less to the micro-organisms than to ptomains present in the pus. He believed that they were dealing with a purely chemical peritonitis.

The principle which Bumm had laid down, namely, that peritoneal infection after gonorrhœa was more apt to occur after menstruation, parturition, &c., soon became emphasized by the reports of cases in the literature tending to disprove the common belief that the infection to involve the general cavity must be a mixed one. The observations alluded to did this, however, more because of negative findings of the pyogenic group than by any positive demonstration of the existence of the gonococcus alone.

Veit,* in 1893, reported five cases in which the symptoms of acute diffuse peritonitis had occurred in women in child-bed, who had become infected in two instances shortly before the confinement and in three during the puerperium. In these cases after a stormy period of a few days the threatening symptoms disappeared, leaving a condition of chronic gonorrhœal pyosalpinx. Veit declared that the peculiar anatomical condition present in the puerperal state occasioned the rapid onset of the peritonitis and offers the suggestion that possibly the lochia affords a good culture medium for gonococci, a view which Bröse† holds because of the observation that one often finds during the child-bed period, the gonococci in great abundance in old infected cases which previously were in such a quiescent state that few, if any, organisms could be demonstrated in the discharges.

Penrose‡ reports a somewhat similar case of a colored woman who, four weeks after her confinement, contracted an acute gonorrhœa, which was followed in six days by symptoms of acute peritonitis. A laparotomy was performed disclosing general peritoneal involvement with a recent double salpingitis. Both tubes were removed. Unfortunately the value of this case was lost by the failure to investigate the bacteriology of the peritonitis and the uncertainty of the pathological report on the tissues which had been removed.

Chaput,§ also cites a case in a girl of seventeen, in whom a general peritonitis followed a double pyosalpinx. The abdominal openings of the tube were patent, and pus could be squeezed from them. The patient died of "paralysis of the intestine." Chaput considered the case an example of general gonococcal peritonitis.

Körte‖ also, in his second report on peritonitis, describes a case (No. 20) in which a general peritonitis, sudden and with great collapse, followed the rupture of a pyosalpinx. The patient recovered after the laparotomy which disclosed a pronounced degree of peritonitis in the exudate of which a few intracellular diplococci were found. Unfortunately they could not with surety be demonstrated to be gonococci.

In 1896, Bröse¶ reported two cases of non-puerperal peritonitis for which he held the gonococcus alone responsible. As in Menge's case, referred to above, the cause of the peritonitis on one occasion was the rupture during manipulation of a small gonorrhœal pyosalpinx. Signs of collapse and

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*Menge, K. Ueber die gonorrhoische Erkrankung der Tuben und des Bauchfells. Zeitschr. für Geburtschülfe und Gynäkologie, Bd. XXI, 1, p. 119, 1891. Ref. Centralbl. f. Gynäkologie, Bd. XVII, p. 457, 1893.

†Zweifel. Verhandlungen des X. Internat. Medic. Congresses, Berlin, 1890. Bd. III Abeth. 8. Gynäkologie, p. 176, 1891.

‡Charrier, P. De la péritonite blennorrhagique chez la femme. Thèse de Paris, 1892.

§Menge. Ueber Laparotomie bei geborstener Pyosalpinx. Centralblatt für Gynäkologie, Bd. XVII, p. 457, 1893.

*Veit, J. Frische Gonorrhoe bei Frauen. Dermatologische Zeitschrift, Bund. I, p. 165, 1893.

†Bröse, P. Ueber die diffuse gonorrhoische Peritonitis. Berliner klin. Wochenschr., Bd. XXXIII, p. 779, Aug. 31, 1896.

‡Penrose, Chas. B. Acute Peritonitis from Gonorrhœa. Medical News, Vol. LVII, p. 16, July 5, 1890.

§Chaput. Péritonite blennorrhagique, etc. Bulletins de la Societé Anatomique de Paris. Annee 69, p. 9, 246, 1894.

‖Körte, W. Weitere Bericht über die chirurgische Behandlung der diffusen Eiterigen Bauchfellentzündung. Mitteilungen aus den Grenzgebieten der Medizin und der Chirurgie, Bd. II, p. 167, 1897.

¶Bröse, P. Loc. cit.

general peritonitis followed. In the light of Wertheim's and Veit's observations, Bröse, although urged to intervene, withheld operation, and after four days the symptoms subsided. His second case was one of a spontaneous rupture of a gonorrhœal tube. Here also extreme symptoms, not only of pelvic, but of a generalized inflammation with profuse vomiting, extreme meteorism and collapse so marked that the case looked hopeless, followed. Again operation was withheld, and by the sixth day all symptoms had subsided. Bröse naturally believed that these peritonitides, differing so greatly in their course and prognosis from the ordinary streptococcus and staphylococcus invasions, represented a distinct form of peritoneal infection. Their symptoms, such as great pain, general tenderness, vomiting, meteorism, singultus, high temperature, small and frequent pulse, are the same as those of general peritonitis from any cause. Their prognosis is however widely different, as complete recovery, except for the chronic condition left in and about the appendages, is the usual outcome. He acknowledges, however, that as no case has been confirmed by section, the pathologic anatomy and the bacteriology of "gonorrhœal peritonitis" are only matters of conjecture.

During the discussion* which followed Bröse's report, the apparent verdict was "not proven." Dührssen believed that he had seen two cases similar to those reported, and he had treated them also in an expectant manner. He regarded the fresh cases, where only endo-salpingitis existed, as the most dangerous for the production of general peritonitis, for in them the abdominal ostia are not closed. A previous pyosalpinx with adhesions naturally renders its occurrence less likely. Baginsky, at this time reported a fatal case in a child following a vulvo-vaginitis of gonorrhœal origin. Unfortunately no note was made on the bacteriological findings of the peritoneum at autopsy. Kiefer expressed doubt as to the extent of the process in Bröse's cases, believing that a local peritonitis might have given similar symptoms. He truly said, "Einen wirklich einwandfreien Fall von diffuser gonorrhöischer Peritonitis giebt es bis jetzt nicht."

Bland Sutton† later in the same year briefly reported a case which almost filled the requirements demanded by Kiefer. It was that of a young girl presenting acute abdominal symptoms supposed to be of appendicular origin. On opening the abdominal cavity he found pus leaking from the ostia of the tubes, which were as large as the thumb, and a general peritonitis of a peculiar form with free purulent fluid described as "gummy." This fluid contained "myriads of micrococci and an abundance of gonococci." The patient was found subsequently to have had a vaginal discharge for three months.

The infection here was regarded as a mixed one, though the variety of "micrococci" was not given. Bland Sutton's report is brief, and no note is made concerning any relation to catamenia or other ætiological factor in the spread of the infection.

If this case is to be regarded as one of general gonococcal peritonitis, it and Wertheim's (l. c.) are the only two which I have been able to discover in a careful search of the literature which carry any convincing proofs of such an origin.

It is hoped that the two following cases, in which the condition was unsuspected and the diagnosis not made until the gonococci were demonstrated in the abdominal cavity, are sufficiently conclusive to establish beyond question the existence of a diffuse pure gonococcus peritonitis.

Case I.—Surg. No. 7719.—*Acute Abdominal Symptoms during Menstruation and following Gonorrhœa. Laparotomy. General Peritonitis. Recovery.*

Mollie C., a maid, aged 25 years, was admitted to Dr. Osler's service May 20, 1898, complaining of abdominal pain.

Her history given on admission was without note. There was nothing to call attention to any pelvic disturbance. She denied the possibility of gonorrhœal infection, and a cursory pelvic examination was negative. Catamenia had always been regular.

The patient stated that four days previously her usual menstrual period had begun. Two days later after an exposure to cold, having fallen asleep in a draught while drying her hair, the flow partially ceased. The same day she began to have some sharp colicky pains in the abdomen and back, but kept at work until the day before admission, when the pain became more severe and quite constant. She remained in bed. Her bowels were constipated. She had some pain in the abdomen during evacuation of the bladder. The next day she was admitted to the medical wards from the dispensary by Dr. Frank R. Smith.

On admission the patient was very much excited and restless, and the history and examination were equally unsatisfactory. The temperature was 100.5°; pulse 110, of good quality; respiration not accelerated. A leucocytosis of 19,000 was present. She was flushed and had a thickly coated tongue. She lay with her knees drawn up.

The abdomen was symmetrical, somewhat full in the umbilical region. Liver dullness extended from the sixth rib to the costal margin. Neither liver nor spleen were palpable. There was no dullness in the flanks; no rose-spots. The only areas of tenderness which the patient acknowledged were in the upper zone of the abdomen. Some muscle spasm was elicited on palpation there. There was no rigidity. Rectal and vaginal examinations were negative (though the patient subsequently said they gave her great pain).

The following day the symptoms became more pronounced. General abdominal tenderness was more marked; the temperature rose to 102.8°, the leucocytes to 22,000. She was transferred to the surgical side for exploration.

Operation May 21, 1898, ether anæsthesia.

Median exploratory laparotomy. General peritonitis. Acute double salpingitis. Gonococci demonstrated. Salpingectomy. Peritoneal toilette. Drainage.

An incision was made through the inner border of the right rectus muscle. On opening the peritoneal cavity no free fluid, but a deeply injected serosa quite universally covered with a deposit of yellow fibrin, was found. The appendix was immediately sought for. It was deeply injected and covered with flakes of "lymph," but there was no evidence of perforation, adhesions or anything identifying it as the source of trouble. Cultures and coverslip preparations were made from the surface of the appendix, and a flake of fibrin was removed for examination. While the coverslips were being examined a systematic examination of the abdominal viscera was made.

* Berliner klin. Wochenschr., Bd. XXXIII, p. 261, Mar. 23, 1896.

† Sutton, J. Bland. Some interesting pelvic cases. Brit. Med. Journ., Vol. II, p. 1309, Oct. 31, 1896.

The serosa of the uterine appendages and pelvis presented no evidences of an older process than that covering the appendix and right iliac fossa. The incision was enlarged and the small, bowel evertrated while the region of the stomach, liver and gall-bladder were explored. No perforations could be found. There was the same injection and deposit of lymph everywhere. The under surface of the liver was covered quite uniformly with a thick deposit. The coverslip examination meanwhile was reported as showing a deeply staining biscuit-shaped coccus, for the most part intracellular, occurring in pairs and not decolorizing by Gram's method. This led to a further examination of the Fallopian tubes. Like the rest of the exposed viscera, they were deeply congested and quite abundantly covered with lymph; they were somewhat swollen, but not markedly so. There were no adhesions of any note about them, and the fimbriæ were free. Both appendages presented the same appearance. On gently squeezing the tube and stripping it toward the free end a thick drop of purulent material could be made to appear much like that seen at the external meatus in gonorrhœal urethritis in the male. An abundance of organisms with the morphology of gonococci were demonstrated in the pus.

Both tubes were removed. The abdominal cavity was thoroughly irrigated with salt solution, and much of the lymph wiped away with salt sponges. The abdominal wound was partly closed, and two drains of gauze wrapped in rubber protective were left leading to the stumps of the tubes.

The patient was quite ill for two days after the operation; restless, with dry tongue, meteorism, vomiting and general appearance of peritoneal infection. She subsequently made a complete recovery. The protective wicks were withdrawn on the fourth day and the wound closed immediately. Doubtless the drainage was unnecessary.

There was a little irregular bloody discharge from the vagina, with some leucorrhœa for a few days. No organisms could be positively identified as gonococci in the urethral or vaginal secretions.

After the operation this additional note was obtained from the patient. She had been exposed to infection for five years or more, and for two years had had some menstrual irregularity, the flow at times being replaced by leucorrhœa. For some months she had had quite a profuse leucorrhœa and considerable burning pain with micturition. She had been exposed to re-infection a few days before her menstrual period.

BACTERIOLOGICAL REPORT BY DR. HUGH H. YOUNG.

Peritoneum—Smears and cultures were made from the large flakes of fibrin which were adherent to the intestines; very little fluid pus present. The smears showed pus cells and fibrin without bacteria. Cultures made on agar slants are negative after several days in the thermostat.

Cultures on ascitic-fluid agar (inoculated with pus and fibrin which had been on an agar-slant for twenty hours) show no growth after many days in the thermostat.

Fallopian tube; surface burned; tube incised with sterile knife. Smears from pus show leucocytes and epithelial cells, and numerous bacteria resembling morphologically the gonococcus. Most of them are inclosed within leucocytes in numbers varying from two to sixteen, typical biscuit-shaped, grouped generally in pairs, sometimes in tetrads. No other bacteria present. After Gram's stain all are discolorized.

Diagnosis, *gonococcus*.

Cultures were unfortunately not taken from the tubes.

Note.—The negative result of inoculations of large amounts of fibrin and pus from the peritoneal cavity upon ordinary agar slants practically excludes the possibility of the presence of the ordinary organisms of peritonitis.

The absence of growth on ascitic-fluid agar signifies nothing, as the medium was inoculated from the surface of an agar-slant twenty hours old. While the positive cultural evidence of the presence of the gonococcus in this case would have been desirable, the certain identification of the organism in the tube and the absence of growth on the ordinary media makes the diagnosis of gonococcus infection convincing.

The demonstration in this case of gonococci on coverslip preparations from the peritoneum made and examined during the operation showed that the peritonitis was not simply of a chemical nature, as the negative cultural findings upon the ordinary media inoculated in the operating room might otherwise have led us to believe. The routine immediate examination of the flora of the exudate in cases of peritonitis often is of the greatest service to the operator, and may give a distinct clue to the prognoses and proper treatment of the case. Had no such examination been made in this instance possibly the source of the infection might not have been recognized, and not improbably the peritonitis have been regarded as a chemical one, as Menge believed it to have been in his case. Negative bacterial results have characterized nearly all of the observations previously mentioned in this report, except the experimental ones of Wertheim. Whether "chemical" peritonitis, so-called, has any actual existence remains a question of doubt. Tavel and Lanz* recognize such a condition, while Flexner† has never failed to find organisms in his 106 cases of peritonitis examined after death. The pathologist doubtless may be less likely to encounter these rather benign cases than the surgeon, but it is possible that some of the "chemical" cases described by surgeons may be, after all, of bacteriologic origin, though difficult to recognize, as was the one here reported.

Case II.—Surgical No. 7760.—*Acute abdominal symptoms during menstruation simulating appendicitis. Laparotomy. General peritonitis. Recovery.*

M. B., a factory girl, aged 18, was admitted to Dr. Osler's service May 30, 1898, complaining of pain in the right side of the abdomen, with persistent nausea and vomiting. The meagre history relative to her condition which could be obtained at entrance was as follows: Six days previously she was awakened in the morning with abdominal pains so severe that she could not get up. Up to this time she had been perfectly well. Her bowels were constipated for some days after this onset, and she had been constantly nauseated with frequent spells of prolonged vomiting, which had increased of late. She had been hiccoughing some. All disturbance with micturition and menstruation was positively denied at this time. Her pain had been constant and always in the right

* Tavel, E., und Otto Lanz. Ueber die Aetiologie der Peritonitis. Mittheilungen aus kliniken und medicinischen Instituten der Schweiz, I Reihe, I Heft., 1893.

† Flexner, Simon. The Etiology and the Classification of Peritonitis. Philadelphia Medical Journal, Nov. 12, 1898.

iliac fossa. She had had no chill and was unaware of any pyrexia. Her general appearance was that of collapse, with peritonitis.

She was seen by Dr. Halsted in consultation with Dr. Thayer, and a provisional diagnosis was made of general peritonitis presumably of appendicular origin.

She was immediately taken to the operating room, where the following note was made before anæsthetization: "The patient is a young woman with flushed cheeks, a thickly-coated tongue and a general appearance of acute toxæmia. Her respirations are costal in type, somewhat accelerated—thirty-four to the minute. Pulse is 100, rather small, but regular and fairly good quality. Temperature is 98.6°. Her extremities are cold, but not clammy as from collapse. There is a leucocytosis of 26,000.

Abdomen.—There is no distention. On the left side there is no rigidity or muscle spasm and no apparent tenderness. Tenderness on the right side is marked, but protective spasm is not a prominent feature. There is a definite point of tenderness two or three centimetres to the right of the umbilicus on a line to the anterior spine. Percussion note has about the same quality over the whole abdomen, with no dullness in the flanks."

The patient insisted that her chief tenderness was in the epigastric region. A vaginal examination which had been made in the ward previously was reported as negative, except for an absent hymen and slight vaginitis.

Operation May 30, 1898, 2 P. M. Ether anæsthesia.

Exploratory laparotomy. General peritonitis. Gonococci demonstrated in exudate. Double salpingectomy. Irrigation and drainage.

An incision was made over the site of the appendix. On opening the peritoneal cavity the whole serosa was found greatly injected and quite uniformly covered with a layer of fibrin. There was no free fluid; no pus. The appendix was found to be deeply congested and covered with "lymph," but in no respect differing from the appearance of the rest of the bowel. The distribution of the exudate was so uniform that (as in Case 1) there was nothing to draw attention to any particular organ in searching for the origin of the peritonitis.

The under surface of the liver, the spleen, stomach and pelvic viscera, all were deeply injected and more or less thickly covered with exudate. This seemed especially abundant on the under surface of the liver, from which it could be peeled off in large flakes, leaving a raw surface exposed.

The tubes were examined early in the search, as the peculiar character of the peritonitis resembled so closely that seen in Case I. They were, like the appendix, congested and covered with lymph, but the fimbriæ were free and there was no evidence that the pelvic peritonitis antedated that in the upper portion of the abdomen. Only after a careful examination of the gall-bladder, stomach, mesenteric glands and bowel were the tubes re-examined when, with some difficulty, it was found that a purulent drop could be brought to the abdominal ostium.

Coverslip preparations were immediately made from this pus, and a biscuit-shaped diplococcus decolorizing by Gram's method was demonstrated in moderate numbers. Cultures were made on various media from this material and from different parts of the abdominal cavity, and a sheet of fibrin about three centimetres in diameter was stripped from the under surface of the liver for future study, and by chance was dropped in a bouillon tube.

Both tubes were removed, the pelvis was carefully wiped out with saline sponges, the intestines irrigated and much of the thick fibrin sponged off. The abdominal wound was partly closed, leaving a small drain leading into the pelvis.

The patient made a satisfactory and complete recovery.

An attempt, made subsequent to the operation, to demonstrate gonococci in the vaginal discharge was unsuccessful. The following important feature of the history was obtained after the operation. She had been frequently exposed to infection for a year and had had considerable leucorrhœa for six months, with some burning and cutting pain during micturition. Several days before her last menstrual period she was re-exposed after a long interval of freedom, and had a return of abundant discharge. Menstruation began as usual, but ceased after three days with the onset of the abdominal pain and vomiting, leucorrhœa and ardor. The patient to protect herself had referred her pain to the epigastric region, and denied any tenderness on pelvic examination.

The appendicular tenderness is an interesting feature. Possibly the great congestion of the organ may have been responsible for the tenderness on pressure near McBurny's point.

RACTERIOLOGICAL NOTES BY DR. YOUNG.

May 30, 1898—A coverslip preparation from the purulent contents of the right tube shows many pus cells and a considerable number of diplococci, with typical morphology of the gonococcus, mostly intracellular. Some cells contain a number of cocci, one showing as many as twenty-five. All completely decolorized by Gram's method.

Diagnosis, *gonococcus*.

Smear from peritoneal cavity (poor preparation; stains badly) shows four typical gonococci, all intracellular; too few to decolorize.

Cultures: 1. Bouillon culture from pus from peritoneal cavity shows no growth after three days in thermostat.

2. Another bouillon tube, into which a large mass of fibrin stripped from the under surface of the liver was dropped, shows slight cloudiness in the bouillon at the bottom of the tube (around the fibrin) after three days in the thermostat. Coverslips made from this show numerous, fairly large diplococci, biscuit-shaped and otherwise typical, morphologically, of the gonococcus. Numerous coverslip preparations were made, and all show diplococci in great numbers and nothing else. All decolorize by Gram's method.

Cultures from this bouillon and also from the fibrin show no growth on ordinary agar after many days in the thermostat.

3. A hydrocele fluid-agar tube was inoculated with a small mass of fibrin which was removed from Douglas' pouch. After twenty-four hours in the thermostat five small, transparent, pin-point colonies were seen on the surface of the medium adjacent to the fibrin. At the end of forty-eight hours they are as large as a small pin-head and semi-translucent in appearance.

Slide-smear preparations show diplococci, morphologically the same as gonococci in pairs and tetrads. All are completely decolorized by Gram.

Transfers on agar from colonies on the hydrocele-agar show no growth after many days in the thermostat.

Diagnosis, *gonococcus*.

Note.—The growth of the gonococcus in ordinary bouillon into which a large mass of fibrin had been dropped is interesting. As is well known, the gonococcus grows well in Marmorek's human serum bouillon (composed of one-third human blood-serum and two-third bouillon) and it seems probable that the fibrin in this instance added the chemical ingredients which sufficed to convert the ordinary bouillon into a fluid resembling this mixture.

The growth was very abundant, and the typical morphology,

decolorization by Gram, and negative growth on agar made the diagnosis of gonococcus positive.

The fact that this culture was taken from just beneath the liver is also conclusive evidence that the gonococcus infection was general throughout the peritoneal cavity.

The similarity of these cases is very striking. In both there was a diffuse involvement of the general peritoneal cavity occurring during menstruation and following a recent exposure to infection associated with the exacerbation of a preëxisting leucorrhœa. Apparently the uterus and tubes at such a time are less able to resist invasion, and an acute gonorrhœal process may the more rapidly ascend from the cervix through the patent abdominal ostia to the serosa. In both cases the onset of abdominal symptoms was sudden with pain and vomiting, but without the shock and collapse seen in perforative peritonitis. In neither case was abdominal tenderness a marked feature, nor was there any distention from paralysis of the bowel as would have been expected with such a pronounced degree of peritonitis under ordinary circumstances. No information was gained by pelvic examination, as both patients concealed the nature and seat of the trouble. The examination of the appendages, however, under more favorable circumstances would have been negative, as the tubes were patent and there had been no accumulation in the lumen. Leucocytosis was pronounced in each case.

The character of the peritonitis in both was the same; a dry fibrinous peritonitis having, as Bröse has said, a distinct individuality. There was practically no pus or serous exudate. In the pelvis there was no evidence that the process had been of longer duration there than elsewhere. The whole serosa was uniformly injected and the deposit of fibrin on the liver and spleen was so thick that it could be stripped away, showing that there was an extensive dissemination of the infectious agent, whether the gonococcus itself or some chemical product of its growth. The fibrinous pseudo-membrane, however, was not essentially of the adhesive kind. Adhesions even in places where the "lymph" was thickest were not a pronounced feature.

From our knowledge of the self limitation of the gonococcal peritonitides and from Bröse's clinical observations, it seems probable that both of these cases might have recovered without operative intervention, but probably with a following chronic pyosalpinx which would subsequently have demanded operation.

Microscopical sections of the tubes showed, especially in Case I, an advanced degree of endo-salpingitis with leucocytes and broken-down epithelial debris in the lumen, and great congestion of the sub-epithelial tissues, which contained many leucocytes with greatly fragmented neuclei. The tubes in Case II showed a much less marked catarrh; one of them indeed (left), being only slightly abnormal. This case, however, showed possibly the most advanced peritonitis and the more severe symptoms. Attempts to demonstrate the organisms in the stained sections were unsuccessful.

The gonococcus has made a place for itself as one of the most important pathogenic bacteria. Few organisms, not even the bacillus typhosus, rival it in the number of suppurative sequelæ which may follow a primary infection. Its occurrence in the conjunctiva, and in the iris, the joints, bursæ and tender sheaths; its occasional demonstration, as the cause of endo- and pericarditis, pleuritis and phlebitis, and the recent observations of cases of pure septicæmia* with its cultivation from the blood shows that its possibilities for metastatic complications are as numerous as are those arising from the spread of infection by direct continuity of surfaces. A general peritoneal involvement by direct extension of an unmixed gonorrhœal process, though long considered among these possibilities has heretofore remained unproven. It adds another variety to the peritonitides of mono-infection which are rare except when of hæmatogenous origin.

Conclusions.

1. The gonococcus is capable of causing a specific infectious disease, namely, gonorrhœa and at the same time other and less specific pathological conditions.
2. There is experimental proof that in certain small animals the gonococcus can set up acute alterations in the peritoneum homologous with the acute septic serositides in man, but differing from these in their tendency to rapid and spontaneous healing.
3. Hitherto there has been wanting conclusive proof that in the peritonitides attendant upon gonorrhœa occurring in women, the gonococcus was solely or chiefly concerned. The inflammations had been variously regarded as mixed infections and chemical inflammations.
4. The cases reported in this paper bring for the first time convincing evidence of the existence of a diffuse, general inflammation of the abdominal cavity caused by the gonococcus.
5. It has been recognized that extension of the gonorrhœal infection from the genital organs to the peritoneum may occur in the puerperal state; a similar sequel is shown to be possible during menstruation.
6. Such ascending forms of gonorrhœa doubtless under ordinary circumstances remain localized in the pelvis, and rarely demand surgical investigation in the acute stage.
7. A general involvement of the peritoneum such as occurred in the two cases given, must either be rare or unrecognized, and may depend upon some especially receptive condition of the serosa or virulence of the organism.
8. The peritoneum is not more immune than are the peri- or endocardium to gonococcal infection, and being more exposed, suffers more commonly in females, although the relatively benign course of the disease makes it a rare condition to come to the attention of the surgeon in the acute stages.

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*Colombini, P. Bakteriologische und experimentelle Untersuchungen über einen merkwurdigen Fall von allgemeiner gonorrhoischer Infection. Centralbl. f. Bakteriologie, u. s. v., Bd. XXIV, No. 25, p. 955, Dec. 30, 1898.

Thayer and Lazear. A second case of gonorrhæal septicæmia and ulcerative endocarditis, &c. The Journal of Experimental Medicine, Vol. IV, No. 1, pp. 81, 1899.

A CASE OF ATROPHY OF THE OPTIC NERVES FOLLOWING HEMORRHAGE FROM THE STOMACH, WITH A CONSIDERATION OF THE CAUSES OF POST-HEMORRHAGIC BLINDNESS.

By Samuel Theobald, M. D.,

Clinical Professor of Ophthalmology and Otology, Johns Hopkins University.

Loss of vision as a consequence of hemorrhage from the stomach is an occurrence of sufficient rarity to warrant the reporting of every well-authenticated case of this character. In a paper upon "Amaurosis and Amblyopia after Hæmatemesis," by Dr. Ed. Pergens, of Brussels, in the January number of the Annales D'Oculistique for 1896, the author, after a seemingly exhaustive search of the literature of the subject, has been able to bring together data of but 64 published cases, two of these being newly reported cases of his own.

The unanimity with which the text-books upon diseases of the eye mention excessive hemorrhage, and especially hemorrhage from the stomach, as one of the causes of optic neuritis, would seem to indicate that cases of this character are of not infrequent occurrence—a conclusion scarcely warranted, I am inclined to believe, by the facts.*

Briefly reported, the case which has recently come under my observation is as follows:

A. B., æt. 57, formerly a lumberman of West Virginia, and more recently a restaurant keeper in one of the small towns of that State, was first seen December 5, 1898. He gave a history of serious disturbance of the stomach of twenty years' duration, the most prominent symptom being frequently repeated attacks of vomiting. On the 6th of May (1898) he had, for the first time, a hemorrhage from the stomach. It was of severe character, and was followed, at intervals of forty-eight hours, by two other equally severe hemorrhages. The loss of blood was so great that his life was despaired of, and he was confined to bed for six weeks. For part of this time (two or three weeks), according to his account, he was in a semi-conscious state—was aware of the presence of people about him and could hear their voices, but could not speak to them or express his wants.

On the day of the second hemorrhage his sight, which had previously been good, became greatly impaired, and his belief is that during the two succeeding weeks he was "entirely blind." At the end of this period his vision began to improve, and he was able to see people moving about the room. This improvement in vision continued, so that by the last of June or first of July he could see well enough to walk upon the streets without guidance; and this amount of vision he retained until about the middle of November, when his sight began again to decline. The decline from this date was pretty rapid, so that when I saw him he had to be led about like one entirely blind. He admitted that he had been a pretty constant smoker, but denied having been a hard drinker, and also denied having had syphilis.

The condition of his stomach was carefully investigated by Dr. Osler and Dr. Thayer, who found a nodular mass near, and partially occluding, the pyloric orifice, which they regarded as the result of a chronic ulcerative process, the indications pointing to a more recent development of a malignant growth in the old cicatricial tissue.

The examination of the eyes gave results as follows: Pupils semi-dilated, somewhat oval in shape and entirely unresponsive to light. The ophthalmoscope showed advanced atrophy of both optic nerves, with some cupping, and marked contraction of the retinal arteries. The optic discs had a woolly appearance, their outlines were irregular and ill-defined, and in each eye there were pigment changes in the retina, not only about the margin of the disc but at points some distance from it and especially in the macula region, indicating that the atrophy of the nerves had been preceded by an inflammatory process which had involved the retina as well as the optic nerves. Upon testing his vision, I found that with each eye he was able to count fingers at about 12″, but only in a very limited part of the field, which in each eye was slightly to the temporal side of the central fixation point.

After an interval of eight days, he having meantime been under treatment in the Johns Hopkins Hospital, he thought his sight somewhat better, and I found that he could then distinguish with each eye Snellen C. at about 10″. An attempt was made at this time to take his visual fields; but this was very difficult and the result unsatisfactory because of his macula blindness and consequent inability to maintain central fixation. The result obtained in the right eye is shown in the accompanying diagram; the attempt as to the left eye was abandoned. Although there seemed but little probability that his sight could be improved by any plan of treatment, he was placed upon small doses of hydrarg. biniodid. with potassium iodid. and increasing doses of strychniæ sulphas.

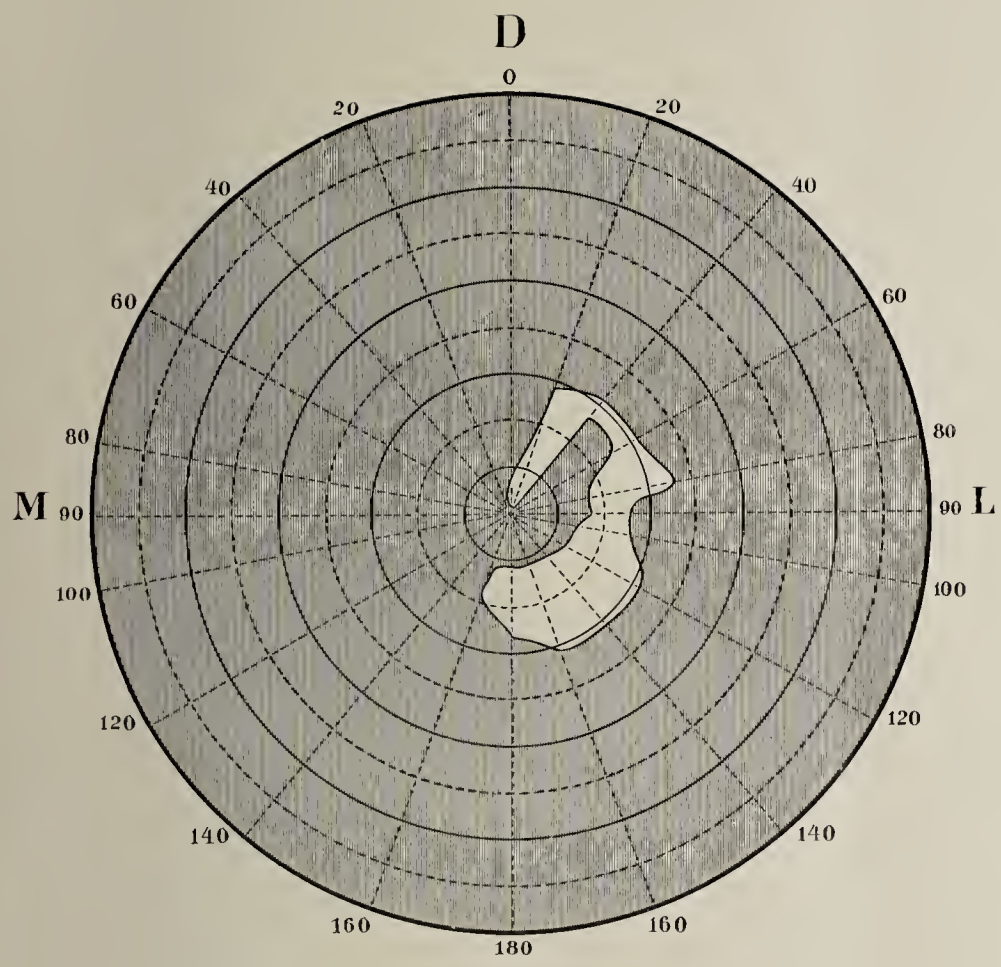
Although, as has been said, the text-books, almost without exception, speak of loss of sight following severe hemorrhage from the stomach, usually ascribing this result to optic neuritis, they have but little to say as to the way in which the loss of blood induces such disturbances in the visual apparatus.

The theory, advocated by Samelsohn* and others, that the optic neuritis is not due to the loss of blood, but that it and the diseased condition of the stomach which induces the hæmatemesis are both dependent upon a central lesion, probably in the optic thalamus, does not seem to be tenable; for we know that other severe hemorrhages, as well as those from the stomach, are followed by loss of sight. Thus Fries† states that while 35½ per cent. of the reported cases of amblyopia from loss of

* I have been able to find in the Catalogue of the Surgeon General's Library, under the title "Inflammation of the Optic Nerve," but a single reference to optic neuritis following hemorrhage.

* Graefe's Arch., Vol. XXI, 1, p. 150.

† Klinische Monatsblätter f. Augenheilkunde, 1878.


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blood were due to hemorrhage from the stomach and intestines, 25 per cent. were due to uterine hemorrhage, 25 per cent. to abstraction of blood, $7\frac{3}{10}$ per cent. to epistaxis, $5\frac{2}{10}$ per cent. to bleeding of wounds, and 1 per cent. each to hæmoptysis and hemorrhage from the urethra.

The theory of Westhoff and Ziegler that the loss of vision is caused by a primary fatty degeneration of the optic nerve induced by ischæmia; as well as that of Hoffman, who attributes the amblyopia and the subsequent atrophy of the optic nerve to a retro-bulbar neuritis, seems to receive but little support from the evidence afforded by the ophthalmoscope in the majority of the reported cases.

In the paper of Pergens, already referred to, a brief abstract is given of each one of the sixty-four cases of amaurosis and amblyopia following hæmatemesis which he was able to find upon record. In a considerable number of them no ophthalmoscopic examination was made; in forty-three instances the ophthalmoscopic findings are given, but the time at which the examination was made varies greatly in different cases.

If we decide, arbitrarily, to regard all the ophthalmoscopic examinations made within three weeks of the onset of the eye symptoms as *early*, and all after this period as *late* examinations, it will be found that 20 of the 43 cases belong in the first category and 23 in the second. The early examinations are, of course, the more instructive. Now, after a careful consideration of the findings in these earlier examinations, it seems to me that, while a very few of them might, perhaps, be cited as supporting the theory of primary fatty degeneration of the optic nerve of Westhoff and Ziegler, the great majority of them point strongly to an obstruction of the blood current in the central retinal artery as the cause of the subsequent intra-ocular manifestations; and, in view of the well-recognized tendency to the formation of thrombi in post-hemorrhagic anæmia, it seems highly probable, if this theory is correct, that the obstruction was of thrombotic origin. This seems the more probable because there is, I believe, a reason why the disposition to thrombosis after loss of blood should manifest itself especially in the retinal vessels.

The occurrence of thrombi after excessive hemorrhage is to be explained by the reduction of blood pressure and the consequent slowing of the blood current, the alteration in the condition of the blood itself (especially the multiplication of the platelets), and, probably, also by changes (consequent upon anæmia) in the vessel walls. Now in the retinal circulation, beside all these general conditions, we have, in the intra-ocular tension, a special condition tending further to obstruct the enfeebled blood current. Here then, it would seem, at the point where the central retinal artery pierces the lamina cribrosa and becomes subject to the intra-ocular pressure, the ideal conditions for the development of a thrombus exist; for here we have the especial point of constriction or obstruction behind which, when other conditions are favorable, a thrombus is prone to develop. The intra-ocular pressure, doubtless, impedes the blood stream in the retinal veins also, but probably not to the same degree as in the arteries.

The ophthalmoscopic picture in thrombosis of the central retinal artery is much the same as is found in embolism of the artery, namely, paleness of the optic disc, marked contraction of the retinal arteries, less marked contraction of the veins, opacity of the retina, especially about the disc and the macula, a cherry-colored spot at the macula, and occasionally, hemorrhages; indeed there are grounds for believing that many of the cases which in the past have been regarded as *embolism* of the central artery of the retina were, in fact, cases of *thrombosis.**

Having in mind this picture, let us consider, more in detail, the ophthalmoscopic findings described in Pergens' paper and see in how far the two agree. In the twenty earlier examinations, which, as before stated, are the more instructive, we find recorded the following conditions:

	Cases.
Arteries contracted	5
Vessels contracted, especially arteries	2
Vessels contracted	2
Arteries filiform, veins very thin	1
Arteries contracted, veins dilated	3
Total in which there is mention of contracted arteries	13
Optic disc, pale	11
Optic disc, greenish-gray	1
Optic disc, clouded	2
Optic disc, clouded and white	1
Total in which there was ischæmia of the disc	15
Cloudiness of the retina	7
" " " with cherry-colored macula	2
White plaques, miliary exudates, etc., in retina	3
Total in which there were characteristic changes in the retina	12
Hemorrhages in retina or upon optic disc	8

Here we have in, at least, three instances the typical picture of obstructed arterial circulation—the case in which the arteries were filiform, and the two cases in which there was clouding of the retina with the red spot at the macula—and in all of the others it is safe to say, I think, that the conditions present may be accounted for more satisfactorily upon this theory than upon any other.

Besides these there are two cases in which the retinal vessels are described as normal (vision being recovered in each); one in which the arteries were slightly enlarged and tortuous and the veins greatly so; one in which the veins were dilated and hemorrhages were present in each eye; and one in which there was a picture of "arrested circulation," all the retinal vessels being increased in size. In the three last-mentioned cases the indications point to interference with the venous circulation rather than with the arterial. This might be explained by the occurrence of a hemorrhage into the sheath of the optic nerve, as suggested by Samelsohn, or by thrombosis of the central retinal vein, although it cannot be said that the characteristic signs of this latter condition were present in any one of these cases. In this connection, however, it is of interest to mention a case of marked impairment of vision following a severe uterine hemorrhage, observed by Dr. Harry Friedenwald, of Baltimore, in which the ophthalmoscope showed in each eye the typical picture of thrombosis of the

* Kern. Zur Embolie d. Art. centr. Retinæ. Inaug. Diss., Zürich, 1892.

central retinal vein. The vision of one eye was regained, but that of the other was permanently lost.

As to the evidence afforded by the ophthalmoscope in the twenty-three cases described by Pergens in which only a late examination was made, it cannot be claimed that it throws much light upon the question under consideration; for the atrophied nerves and contracted arteries usually mentioned as present might have been due to other conditions as well as to thrombosis of the central artery, and this is equally true of the case which I have reported.

The character of the visual field in my case, as well as that in several of the small number of cases in Pergens' paper, in which the field is described (vision having been retained only in a circumscribed area in the temporal field) is significant, and seems to point to the partial preservation of the retina in the neighborhood of the papilla by means of the cilio-retinal arteries.

Of the whole number of cases collected by Pergens, autopsies were made in but four. In one of these a thrombosis of the splenic artery was found, but no mention is made of the condition of the eye. In a case reported by Hirschberg* there was complete atrophy of the optic nerve of one eye, and atrophy of a limited portion of the optic nerve of the other eye. In the affected portion of the nerve there were numerous blood-vessels with thickened walls but no thrombosis and no signs of hemorrhage in the optic nerve sheath. The death of the individual, it should be stated, did not occur until three years after the loss of vision.

In an autopsy by Ziegler,† twenty days after the attack which led to loss of vision, no macroscopic changes in the optic nerves or their sheaths were found; but the microscope showed fatty degeneration of the nerves and their intra-ocular expansion.

The only other autopsy was one made by Raehlmann.‡ All the arteries presented constricted lumina from a fibrous endarteritis. The veins also had undergone slight constriction, in two places being almost totally obliterated. There was œdema of the retina, especially in the neighborhood of the disc. In the choroid the endarteritis was pronounced and there was hyaline degeneration. Here, too, it will be seen, we have mention of vascular changes, the thrombosis of the splenic artery in the first-mentioned case being, at least, suggestive, and the condition of the retinal vessels and of the retina itself in Raehlmann's case being especially significant.

The fact that both eyes are so frequently involved in blindness dependent upon acute anæmia* seems, at first sight, to make against the theory that the loss of vision is due to thrombosis of the central retinal artery, since it implies the occurrence nearly simultaneously, at different points, of two thrombi; but, if the intra-ocular tension plays as important a rôle in the etiology of these cases as I believe it does, this objection loses much of its force.

Conclusions.

1. That the weight of evidence afforded by the ophthalmoscope points to thrombosis of the central retinal artery as the usual cause of the blindness which occurs in post-hemorrhagic anæmia.

2. That the resistance offered to the already enfeebled blood current in the central retinal artery by the intra-ocular tension is an important etiological factor in determining this result.

3. That, in exceptional instances, the ophthalmoscope indicates that the thrombosis occurs not in the artery but in the central retinal vein.

4. That, in other exceptional instances, it may be that the loss of sight and the ophthalmoscopic changes which accompany it are the result of a hemorrhagic or serous effusion into the optic nerve or its sheath (Samelsohn). And here, again, the obstruction and damming back of the blood current in the central retinal artery by the intra-ocular tension, probably, have much to do with bringing about this result.

* Zeitschr. f. klin. Med., Vol. IV.
† Ziegler und Nauwerck's Beitr. z. path. Anat., Vol. II.
‡ Fortschr. d. Mediz., 1889, p. 928.

* Whether one or both eyes were affected is stated in fifty-seven of the cases collected by Pergens. Of these, both eyes were involved forty-nine times; one eye only eight times.

LICHEN SCROFULOSORUM IN A NEGRO.

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(*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*)

This case is of interest not only on account of its great rarity in this country, only four cases having been previously reported, but also because it is the first recorded instance in the negro. In the four cases already reported, one of which occurred in Canada, no microscopical examination was made.

While attending a number of negro children in an orphan asylum for tinea tonsurans, one young girl, eleven years of age, was brought to me with some lesions on the back and thighs which the attendant thought were ringworm patches and which had been noticed a few days previously. The patient appeared to be a healthy, well-nourished girl; she was not anæmic, did not complain of anything, had a good appetite but was rather quiet in her manner. The tongue was clean. On examination there were found on the upper portion of the back a number of round and oval patches varying from about 10 to 20 mm. in diameter. A few similar patches were found on the extensor surfaces of both thighs, about the left groin, on the anterior surface of the right thigh and in the

pubic region. The patches all consisted of groups of small, conical, slightly scaly and therefore whitish firm papules, each papule being about 0.5 mm. in diameter, raised and presenting a flattened summit which was covered with a somewhat adherent but not profuse whitish scale, on removal of which a bleeding surface was exposed. The papules presented in every patch exactly the same character and were always discrete and of the same size. There was a slight red areola surrounding the base of the papules. The most recent patch presented a group of seven rather closely aggregated conical papules which were not scaly. The oldest groups which were in the groin were much larger and the central portion appeared to be clearing up, although on close examination one could still detect the remains of slightly scaling papules which were much flattened. Many of the lesions were pierced by lanugo hairs and were therefore situated around hair follicles. Two patches on the left groin were becoming confluent and thus formed an irregularly shaped area.

This case was not diagnosed absolutely at first, and numerous scales were examined in the usual way for the ringworm fungus but no evidence of any mycelium or spores could be found. The patient was seen every other day and numerous new lesions were observed developing, especially on the back as well as on the abdomen, forearms, and arms. Five weeks after the first appearance of the eruption a typical phlyctenular conjunctivitis of the right eye developed. The diagnosis was confirmed by Dr. Theobald. The distribution of the lesions at this time was as follows: A few scattered patches on the extensor surfaces of the forearms and arms; 4 patches on the right side of the chest; 5 scattered areas on the abdomen between the umbilicus and pubes; nearly 60 groups distributed over the whole back; a few extensive patches on the extensor surfaces of both thighs and numerous areas in both groins. The head, neck, hands, legs and feet were all clear.

Patches which were only two days old were seen to consist of from four to seven, conical but flattened, firm, non-scaly papules, some arranged around, others between the hair follicles. Many of the lesions presented the appearance of a keratosis pilaris. The papules always appeared in the same way, gradually developing whitish, but not profuse, adherent scales, on removal of which a bleeding surface was exposed. The patches were gradually increased in size by the addition of new papules around the periphery while the older central lesion gradually flattened but remained scaly. The lesions then assumed a circular or oval-shaped aspect with a cleared-up center. The long axis of the patches in the lumbar region was transverse to the body. When two adjoining patches approached one another the intervening papules showed a tendency to gradually disappear, but over the region of the right scapula there was a large irregular area of papules which was made up of 10 groups, none of which had cleared up in the center. A whitish collarette extended up the hairs in many of the papules in the lumbar region. No vesicles or pustules were observed clinically during the course of the disease. A few solitary papules could be detected scattered over the back. All varieties of the lesions are well shown in the photograph (Fig. I) especially if a hand magnifier be used. There were no subjective symptoms.

A probable diagnosis of lichen scrofulosorum was made at first which was confirmed by the extension of the lesions, their uniform character and the appearance of a typical phlyctenular conjunctivitis. Numerous enlarged lymphatic glands were also present but as they occur often in healthy negroes, this symptom was not regarded as important.

The patient is the fifth of eight children (five girls and three boys), all living and in good health with the exception of one girl who died of "consumption." The father and mother are living and in good health. There is no tuberculosis in any form in the family now living.

Under the internal administration of hypophosphites and cod liver oil the cutaneous and eye troubles both rapidly disappeared. The sections all presented two striking features: (1) semiglobular-looking masses situated in the horny layer and in the majority of instances around the hair follicles, and (2) marked pathological changes in the upper portion of the corium beneath these papular masses and also around the hair follicles, especially the deepest portion. The latter was characterized by its tubercular structure. One could follow in the sections the formation of these clinical papules. Fig. II explains their genesis. The blood-vessels in the upper portion of the corium and papillæ were dilated and many polynuclear leucocytes had wandered out into the tissue and into the epidermis up to the horny layer where these cells became disintegrated; numerous lymphoid cells were found in the same situation, undergoing the same processes. Thus a mass of detritus and an apparent firm ground substance is deposited in the horny layer. This ground substance takes up the eosin stain very readily while the cells take up the hæmatoxylin. There are also a few degenerated epithelial cells in the mass of detritus. The stratum lucidum and stratum granulosum have disappeared. No apparent fluid exudation accompanies this emigration of cells through the rete, and the epidermal cells are but little swollen, nor are the interepithelial spaces much widened. Large numbers of pigment granules are also scattered throughout the papular lesion.

In Fig. III is represented a section of the whole patch excised showing three papules, (*P*) all of which are well marked. One shows its relation to a hair follicle (*P*); from the second it is evident that the section has just passed outside of the follicular opening as evidenced by the presence of the lower portion of the follicle (*H*); while the connection of the third with a hair follicle is seen in another section. The more pronounced papules show that they are made up of the same materials which have already been described, with the exception that there is a larger amount of pigment in the lesions. Directly in contact with the hair (*H*) there is a well-marked hyperkeratosis encircled by the papular lesions. This hyperkeratosis extends nearly half way down to the hair follicle. The middle papule exhibits completely the nature of the lesion just outside of the hair; it consists of a firm substance imbedded in which are enormous numbers of degenerated polynuclear leucocytes, lymphoid cells, many epithelial cells and masses of pigment granules. The mucous layer beneath consists of two layers of cells through which are emigrating hundreds of wandering cells. There is some

widening of the interepithelial spaees, but no marked œdema. The eorium, espeeially direetly beneath the papules and around the hair follicles shows marked changes. In the first region there is a fairly well-defined area eonsisting of the papillæ and upper portion of the corium, in whieh are massed large numbers of lymphoid cells, numerous polynuclear leucocytes and some plasma eells with dilated blood-vessels. (Fig. III, *C.*)

Around the hair follieles in the lower portion are masses of ehiefly round mononuelear eells, some plasma cells and epithelioid eells and a few mast eells. In four seetions typical tubercles were observed in this situation (Fig. III, *G*), with giant eells forming the eenter surrounded by numerous epithelioid cells and mononuelear round cells at the periphery. The hair follicles themselves are unaffected. The blood-vessels (V) throughout the eorium are dilated, are surrounded by numerous mononuelear round cells, a few plasma cells and numbers of polynuelear leucocytes. Two unaffeeted sebaceous glands were seen in one of the seetions. The sweat ducts and sweat glands were normal, although a duct was seen passing close to the lesion. The blood-vessels aecompanying the sweat duct were dilated and surrounded by additional eells as were other vessels. No tuberele bacilli were found in any of the sections stained for this purpose.

Hebra first deseribed the disease and named it lichen scrofulosorum to charaeterize its clinical features. He deelared that it was always aeecompanied by other symptoms of serofula. The disease had been previously deseribed as lichen simplex by Erasmus Wilson, and as liehen eireumseriptus by Cazenave. Jaeobi in 1891 drew attention to the tubereular nature of the lesions, whieh he thought to be a perifollieular tuberculosis of the skin. Although he demonstrated a single tubercle baeillus in one of his sections, an inoculation into guinea pigs gave negative results. Later (1896) he demonstrated the presence of tubercle bacilli in a typical case and obtained positive results in a rabbit. In 1892 Sack decided, after a careful histological examination, that the disease was a miliary tuberculosis of the skin, the nodules showing a central caseation, then giant cells, epithelioid cells and small round eells. He suggested "tuberculosis liehenoides cutis" as a more applieable title. Later observers have apparently demonstrated the tuberculous nature of the affection especially of the severer forms. Thus Jadassohn found in 19 cases 14 associated with tubereulosis, and only one case in which no sueh disease was present. He was of the opinion that the disease was non-baeillary, but that it was a disease of tuberculous persons. Of 16 cases treated with tubereulin 14 reaeted typically, but although inoculations were made into guinea-pigs from nine of the cases, negative results followed. Kaposi believes that there is nothing to prove that lichen scrofulosorum is a manifestation of tuberculosis, although he asserts that tuberculosis is always present. In Tilbury Fox's six cases he noted the presence of tuberculous symptoms in the patients. Pellizarri succeeded in producing tuberculosis in a guinea-pig after the inoculation from one case.

Haushalter (1898) inoeulated 4 guinea-pigs from 2 eases and they beeame infected with tubereulosis, one of the cases had an otitis media, the other a tubereulous lymph gland as well as enlargement of other eervical glands. Some German dermatologists, e. g. Kromayer, Kaposi and Lukasiewicz, are opposed to the tubereular origin of this disease on aeeount of the absenee of easeation, the mildness of the affeetion and the rapid recovery. Only a very few cases have been reeorded in Franee, and in those examined histologieally no tubercle baeilli were ever demonstrated, although the subjects were tubereulous. It was believed, therefore, by the Freneh dermatologists, Hallopeau, Brocq and Bureau that the lesions of lichen scrofulosorum were not due to direct infection bnt rather to the toxin of tuberculosis. Hallopeau reported one ease whieh was assoeiated with lupus. The liehen eruption was seattered ehiefly over the trunk, but one group of papules was situated directly around the lupus nodule which had a scar in the eenter. In Lefebre's ease no bacilli were found in the sections, and the animal inoeulation was negative. In both the eases reeorded by Morris and Crocker tuberculous glands were present, but in Walker's ease tubereulosis in any form was absent, neither was there any tubereulous history.

With referenee to the Ameriean reports, only two cases have been exhibited at the meetings of Soeieties, and of these only elinieal histories have been given. In all the eases recorded, the histologieal findings always show a likeness to those in tubereulosis, but in most instances after diligent seareh no bacilli have been found nor was the disease reproduced in guinea-pigs after inoeulation. The inoeulations, however, which have resulted successfully have demonstrated its tubereulous nature in those eases. My own ease is a comparatively mild one and the presenee of baeilli eould not be demonstrated. Clinieally it presents all the typieal features of a liehen serofulosorum as originally described by Hebra with the exeeption of the color, whieh would naturally differ in a negro's skin. Tilbury Fox ealled attention to the fact that instead of always appearing in gronps, the papules may oecur singly.

Sack in his descriptions and drawings shows that the papule is formed by the miliary tubercle being deposited direetly beneath the epidermis and by some slight hyperkeratosis of the horny layer.

In my ease the papules eonsist of distinet lesions involving the horny layer, and form, as it were, a dry pustule. It was neither elinieally nor histologically a pustnle, sinee it appeared to be made up of a homogeneous ground substanee with masses of nuclear detritus and numerous pigment granules. There was no special hyperkeratosis. The tubereular nature of the disease was far from being pronouneed histologieally in the present ease and the tubereles were situated around the lower portion of the hair follicle.

It is strange that a tubereular eutaneous eruption which yielded so readily to eod-liver oil should arise in a well-fed, healthy ehild with good hygienie surroundings and without previous history of tubereulosis. Clinically the case suggests the adoption of Hebra's title of lichen serofulosorum or Unna's follieulitis serofulosorum rather than tubereulosis follieularis. Since sueeessful inoeulations, however, have been made in at least three cases, then the latter title would be more eorreet.



FIG. I.—Photograph of a case of lichen scrofulosorum in a negro girl. The lesion can be best seen by using a hand magnifier as a small scaly papular eruption.



FIG. II.—Shows a commencing papule (*A*) which is formed between the horny layer (*H*) and the mucous layers (*M*). Numerous polynuclear leucocytes (*P*) and lymphoid cells are emigrating through the epidermis to the horny layer. Two papillæ (*B*) are filled with wandering cells and dilated vessels.



FIG. III.—Shows three well marked papules (*P*, *P*, *P*); one encircles a hair (*H*); in the other two the section has passed outside the follicular opening. *H*, *H*, are hair follicles; *C*, collections of lymphoid, plasma and connective-tissue cells and polynuclear leucocytes; *V*, *V*, dilated blood-vessels; *G*, is a tubercle near the lower portion of the hair follicle *H*; *F*, is fat; *S*, sweat glands; *D*, collection of cells around hair follicle.

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A NEW INSTRUMENT FOR MEASURING HETEROPHORIA AND THE COMBINING POWER OF THE EYES.*

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This evening I wish to describe a new instrument that I have recently devised for the estimation of certain functional disturbances in the extrinsic muscles of the eyes. The instrument is equally usefnl for testing both the heterophoria and the combining power of the eyes, but as one of its main features is that of a phorometer, I shall speak of it as a reflecting phorometer.

The instrument consists essentially of four mirrors, two for each eye, arranged one above the other and mounted in a rectangular frame so as to rotate on axes. The axes of the two upper mirrors are in the same line and are parallel to the horizon and perpendicular to the direction of sight. The axes of the lower mirrors are parallel to each other and lie in planes perpendicular to the horizon, and parallel to the direction of sight. The distance between the two lower axes is 6.25 cm. This distance may be greatly varied without having any material effect on the accuracy of the instrument, but the distance given was chosen as the most convenient one and closely approximates the average distance between the eyes.

The lower mirrors are made as large as possible without their interfering with one another. The upper mirrors are of the same size as the lower except perhaps a little longer. A good size for the lower mirrors is 3 cm. x 5.5 cm., and for the upper mirrors 4 cm. x 6 cm. In this model the axes of the upper mirrors are 5 cm. above the middle points of the axes of the lower mirrors, but this distance is unnecessarily great.

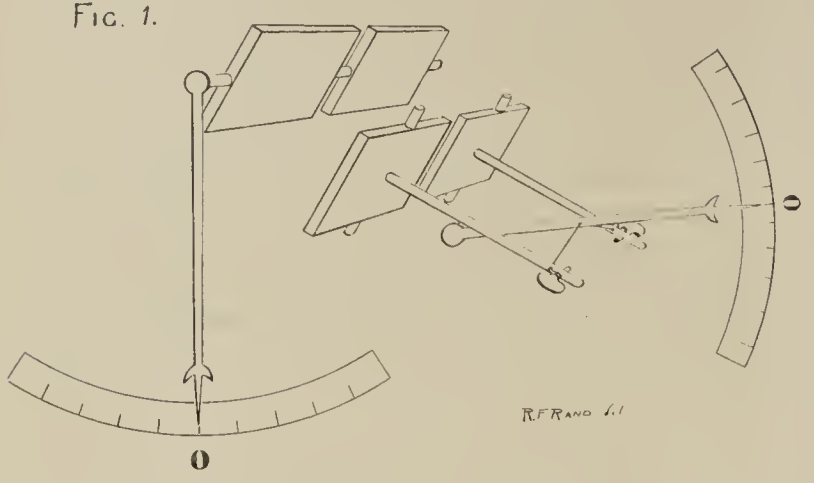
The axes of the lower mirrors are at an angle of 45 degrees to the perpendicular, but I think it would be better to reduce this angle as much as possible. The ideal way would be to have the axes perpendicular, but this is impossible since the lower mirrors would shut off the view from the upper ones. One of the upper mirrors is permanently set at an angle of 43 degrees to the perpendicular, while the other is freely movable about its axis, and to its outer end is attached a lever, 15 cm. in length, which is arranged to move along a scale and mark off the amount of rotation of the lever. Since the angle through which a mirror rotates is half the angular deflection produced in a ray striking it, the scale must be made so that one-half a degree of rotation of the mirror corresponds to one degree on the scale. The scale must be still further changed if it is desired to have it register prism-degrees.

To each of the lower mirrors a lever is firmly attached perpendicular to the axis at its middle point. These levers are each 8 cm. long, and at a point on each, 6½ cm. from the mirror, a small hole is drilled about the size of a cambric needle. Below this another, larger hole is drilled into which a key is fitted similar to those used on violins for tuning purposes. To a partition, placed midway between these levers, is attached another lever 14 cm. in length and pivoted at a point 3½ cm. directly behind a line joining the two levers and extending from the needle hole on one to the similar hole on the other. Three centimeters from the pivot of this middle lever a small hole is bored and a thread is then run through this hole by means of a needle and then continued through the holes of the other two levers. The thread is now connected with the keys on these levers and wound up until it is 3.1 cm. in length on each side. It must be firmly fastened

* Read before the Johns Hopkins Hospital Medical Society, January 23, and before the Maryland Ophthalmological and Otological Society, January 26, 1899.

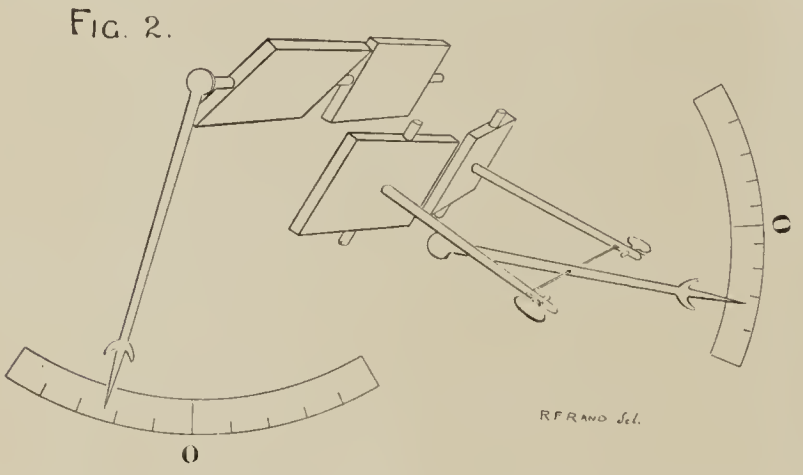
in the hole of the middle lever so that it will not slip. The thread is then made tense by means of rubber bands or helical springs attached to the levers and then to the sides of the frame. The object of the middle lever is to produce equal though opposite angular displacements in the two laterally moving levers.

Fig. 1.



A diagrammatic representation of the arrangement of the mirrors and levers is shown in Figs. 1 and 2. In Fig. 1, the two upper and the two lower mirrors are parallel and hence both scales register zero. In Fig. 2, one upper mirror is rotated to estimate hyperphoria or right sursumduction and the middle lever is depressed, tilting the two lower mirrors towards each other, to estimate exophoria or abduction.

Fig. 2.



A double level is fastened to the top of the instrument and the latter, resting upon a suitable stand (I have been using a camera tripod), is leveled and pointed at a small circular spot, distant twenty feet or more. To find the zero point for lateral displacement, one sights *over* one of the lower mirrors and then *through* this mirror and ascertains whether the image is in line with the object. If not, the middle lever should be moved up or down until this condition is obtained and then zero marked on the scale provided for the purpose. One must then sight over the other mirror in a similar manner, the adjustment being made this time however by the key attached to the lever of this mirror. A one-half degree prism is now held, base in, before one of the mirrors and the image as seen through both prism and mirror is put in line, by means of the middle lever, with the object as seen over them. One degree must now be marked upon the scale since there is a lateral displacement of one-half degree produced on each side. Similarly a scale of degrees for both esophoria and exophoria is obtained. To obtain the zero point for the upper mirrors, the middle lever is pulled down until both images can be seen with one eye and they are then placed on a level by means of the lever attached to one of the upper mirrors. Another method is to put the middle lever at zero and then view a horizontal line with one eye, moving the lever attached to the upper mirror until the line is apparently continuous. By the use of prisms an empirical scale may be obtained by this method.

After the zero point for the lateral displacement is once obtained, it is an easy matter to readjust the instrument if the threads should break or stretch. All that is necessary is to place the middle lever at the zero mark and then turn the keys attached to the levers of the lower mirrors until the object is in line with the images seen through the mirrors.

It is important both in graduating and in using the instrument to have the object at the same height as the instrument and also directly in front of the latter.

At the back of the instrument there is a door with two horizontal windows cut in it so as to correspond to the level of the eyes and their distance apart. On a pivot on the inside of the door is a shutter so arranged that when worked by means of a string it alternately closes one window and opens the other, one being always closed while the other is open. It would be very advantageous to have this shutter worked by some sort of clock-work arrangement.

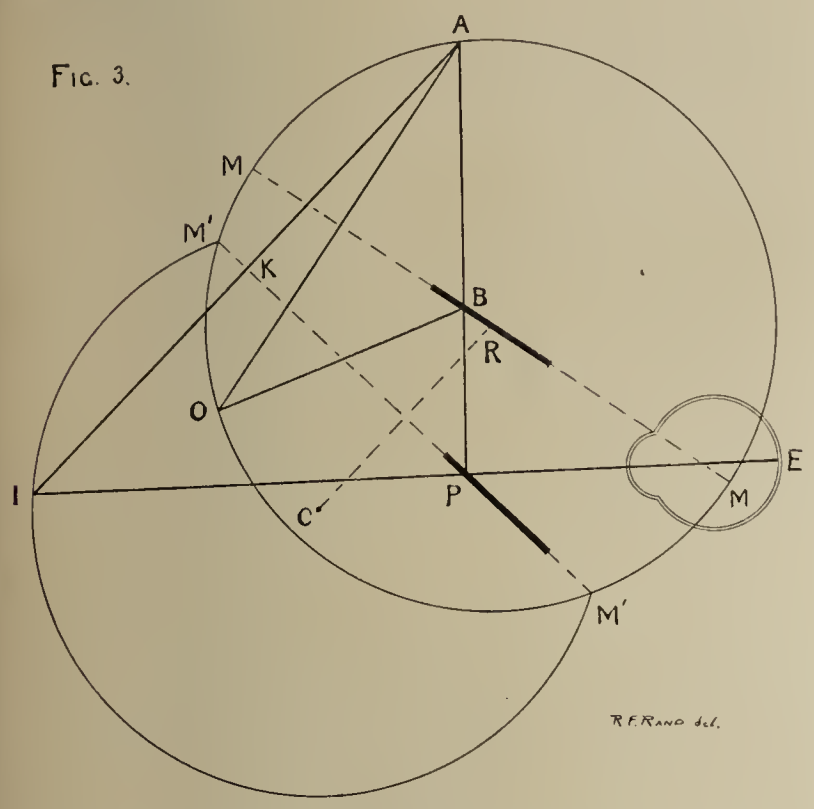
To use the instrument, the patient is directed to sit down behind it, place his eyes on a level with the windows, and look through them at the circular spot, which, as has been said, should be at a distance of about twenty feet. The levers are then placed at zero on both dials and the shutter is moved to and fro at a moderate rate of speed. The patient is now asked to state whether the object seems to move or not. If not, his muscle balance is perfect. If he sees the object apparently moving obliquely, the outside lever, that is the lever attached to the upper mirror, is moved until the patient says the movement is horizontal and then the middle lever is adjusted until there is practically no movement. The outside lever will then register the amount of hyperphoria while the middle lever registers the amount of exophoria or esophoria, according as it is below or above the zero point.

If now it is desired to measure the relative adduction, abduction, or sursumduction of the eyes, that is the combining power of the eyes, the door at the back of the instrument is opened and the patient directed to look through the mirrors with both eyes. He will then see the object single, and without effort, since his heterophoria has been corrected by the previous adjustments. The middle lever is now depressed until the patient, by the greatest effort that he can make, is just able to fuse the images. The dial will then register the number of degrees of abduction. Similarly the amount of adduction and of right and left sursumduction may be obtained.

In addition to the test with the shutter, the amount of heterophoria may be estimated by this instrument in a manner similar to that adopted when prisms are used. To do this all that is necessary is to produce vertical or lateral dip-

lopia by the levers, and then move the proper lever until the images are in line. It is well to use this test as a confirmation of the shutter test.

FIG. 3.



The diagram, Fig. 3, is intended to illustrate in as simple a manner as possible the construction involved in locating the position of the image for each eye. The relations of object and mirrors to each other are exaggerated in order that the construction lines may be more plainly seen. The mirrors are in their primary positions, so that a line drawn perpendicular to the axes of the upper and lower mirrors will be perpendicular to the plane of the lower mirror. *O* is the object, *M* and *M'* the mirrors. From *O*, a line *O A* is so drawn that it is perpendicular to and bisected by the prolongation of *M*. Similarly from *A* the line *A I* is drawn perpendicular to and bisected by the prolongation of *M'* at *K*. All the rays from *O* striking *M* will be reflected in lines directed from *A* and these rays will be reflected from *M'*, in lines directed from *I*. Therefore an eye directed towards the mirror *M'*, will see the image of *O* at *I*. The actual path taken by a ray of light from *O* is indicated by the line *O B P E*. The locus of *A*, as *M* is rotated on its axis, *R*, is evidently the circumference of a circle whose radius is *O R*. The locus of *I* during this rotation is the circumference of a circle with the same radius but whose center is at *C*, *R C* being drawn perpendicular to, and being bisected by, the prolongation of *M'*.

When *M'* is rotated on its axis, which lies in the plane of the construction, it is evident that *I* will move along the circumference of a circle perpendicular to the prolongation of *M'* and whose center is *K*. This circle being at an angle to the line of sight, *I* will apparently take an elliptical path.

From this it will be seen that when the middle lever is moved the image pertaining to each lower mirror moves in the circumference of a circle tilted at an angle of 45 degrees to the perpendicular and whose center is at the foot of the perpendicular drawn from the object to the axis of the mirror. Since the projection of a circle is an ellipse, the image of each mirror will apparently move in an elliptical course, and will thus not only move laterally, but also upwards to a slight extent. This, of course, would seriously interfere with the accuracy of the instrument if each lower mirror were rotated independently, but by the arrangement previously described, both mirrors are made to move equally though in opposite directions and hence the images when viewed with both eyes maintain their horizontality.

If the test object is a perpendicular line its image will generate the surface of a cone and thus when projected the two images, as they are carried apart, will make increasing angles with each other. In this way a certain amount of rotation of the eyes on their principal axes could be measured, and with this model about eight actual degrees of such rotation can be determined. This method is entirely distinct from that just to be described.

The rotation of the eye on its principal axis is spoken of as torsion. Where this rotation remains constant I would suggest that the term torsional strabismus or squint be used. Where the eye has simply a tendency to rotate, the term cyclophoria has been suggested. These conditions may be accurately determined by the following arrangement: Two equal circular disks each having two perpendicular lines drawn through its center are placed one above the other so that one of the perpendicular lines in the upper disk is continuous with one of the lines in the lower. The upper disk is so made as to rotate upon its center when desired and degrees should be marked off upon the background to which it is attached. The lower disk should have its semi-circumference plainly marked off in degrees. The instrument is then pointed at the two disks and the hyperphoria lever so manipulated that the images of the two are exactly superimposed. The patient's esophoria or exophoria should be corrected by prisms.

To measure the amount of torsion the eyes are capable of undergoing, that is, the torsional combining power of the eyes, the upper disk is rotated until the lower or upper lines are beginning to be seen double and the number of degrees read off. To test the torsional squint, the upper disk is rotated until only two lines are seen and the number of degrees read off. To test the cyclophoria it is best to rotate the upper disk a definite number of degrees and then have the patient read off the number on the lower disk as he sees it, the difference between the patient's reading and the number of degrees the upper disk has been rotated will be the number of degrees of cyclophoria.

From a few experiments made upon myself and others, I am inclined to believe that normal eyes have little or no torsional combining power. In the few cases I have examined I have not found the slightest evidence of cyclophoria in the otherwise normal eye. Considering the disinclination of the normal eye to undergo torsion, it seems to me that if cyclophoria were present to any extent it would soon lead to torsional squint and produce amblyopia in one of the eyes.

A certain amount of angular displacement of the *vertical* lines may be produced without diplopia resulting, but this is

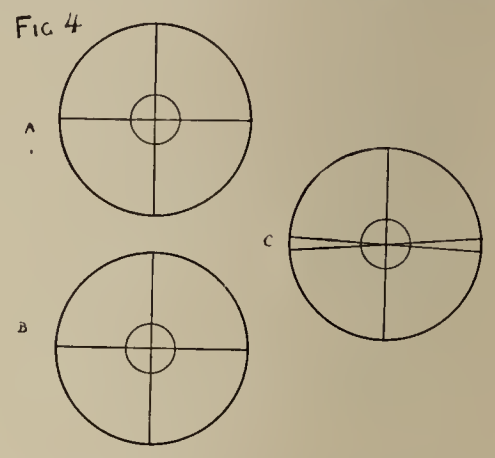
not overcome by rotation of the eye, however, as diplopia is almost immediately produced by the equal angular displacement of the *horizontal* lines. The phenomenon must be due, I think, to a psychical compensation, if I may be permitted to use such an expression.

The reason this psychical compensation is so much greater for the perpendicular lines than for the horizontal is due, I think, to the fact that in viewing perspectives, the eyes have a stimulus to fuse non-corresponding points that are displaced laterally, while there is no call upon them to fuse perpendicular displacements, the eyes being always upon the same plane with regard to each other.

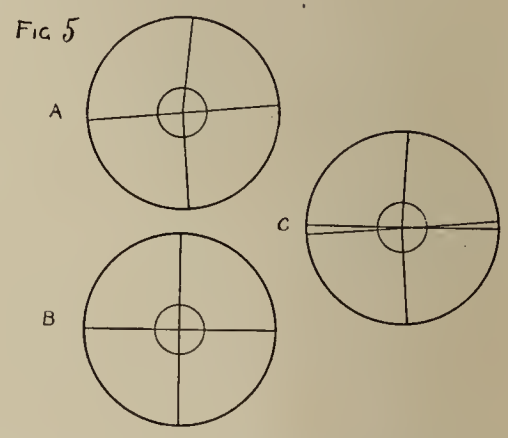
In this connection I quote the following from G. T. Stevens*: "It is an interesting as well as an important practical fact, and one to which little attention has been given, that horizontal lines cannot be held in union while being rotated from the horizontal direction to an extent nearly equal to that in which vertical lines can be held in union. If vertical lines can be held in union with a rotation of 20 degrees or more, horizontal lines become double with a total rotation for both tubes of from 6 to 8 degrees. Indeed, it requires some practice to hold the lines in union with a rotation of each tube either out or in to the extent of 3 degrees."

Stevens made his observations by means of an instrument which he calls the Clinoscope. This instrument enables him to superimpose various figures. The observation just quoted was made by superimposing two straight lines only. Stevens believes the phenomenon is due to differences in torsion, for he says: "A very considerable latitude is permitted in respect to the position of the vertical lines and the torsional act may overcome an important normal deviation." My experiments, however, lead me to believe that what Stevens has been studying is not the amount of torsion, but the variations in the psychical compensation for the different meridians of the eye. I have found that the greatest angle of separation of the lines at which they may still be fused, depends to a certain extent upon their length or what is just the same thing, upon the distance at which they are observed; the greater the distance, the greater the angular displacement allowed. This could not be the case if the phenomenon were due to torsion. On the other hand, if due to a psychical compensation for non-corresponding points, the increase in the angle with the increase in the distance would be expected, since the extremities of the lines would have to be placed farther apart in order for the extremities of their retinal images to be the same distance apart as before the increase in distance.

Another observation that I have made seems to prove conclusively that it is not by undergoing torsion that the eyes combine lines which are placed at an angle to each other. This observation was made by having the upper part of the vertical line on one disk separate from its lower part so that it could be put at an angle to the latter. If the upper part is rotated it will be seen that the line is no longer continuous, but consists of two radii of the disk placed at an angle. This line is readily fused with the vertical line on the other disk even when its two parts are at an angle of more than 10 degrees. It is inconceivable that such a line could be combined with a straight line by a process of torsion, since at least one of the eyes would have to rotate in two opposite directions at one time, but the assumption of the existence of a psychical compensation explains the phenomenon here just as satisfactorily as when both verticals are straight lines.



In Fig. 4 the upper disk, *A*, has been rotated 8 degrees, while the lower disk, *B*, is in the primary position. *C* represents the appearance presented to the eyes when *A* and *B* are superimposed. In Fig 5 the upper and lower parts of the vertical on *A* have each been placed at an angle of 5 degrees to the perpendicular, and are thus at an angle of 10 degrees to each other. The horizontal line remains perpendicular to the lower part of the vertical line and hence has been rotated 5 degrees. *C* shows the appearance when *A* and *B* are superimposed. It will be noticed that the angle between the two parts of the displaced vertical line on *C*, is less than the corresponding angle on *A*.



In the proper use of the reflecting phorometer the shape of the object to be viewed is of very great importance. As mentioned above, when the images are displaced laterally they are also inclined towards or away from each other and consequently it would be impossible to combine them if the object were a line, unless the eye underwent torsion. This, I find, it refuses to do, and it is necessary to adopt a plan to overcome the difficulty. Practically I have found that the images of a small circular spot about 3½ cm. in diameter are readily combined. As a matter of fact, the images of the round spot when lateral separation is produced are converted into ellipses whose axes are inclined to one another, just as in the case of the straight line, but there does not seem to be

* Archives of Ophthalmology, Vol. XXVI, pg. 201.

enough difference in the images to interfere with perfect fusion. Theoretically a sphere should be employed as the object, for no matter how rotated its projection would be a circle. If used, however, it must be evenly illuminated, otherwise the shading would defeat the purpose in view. Lighted candles, of course, cannot be employed. The best arrangement is, either a small white circular spot on a black background of good size, or a lamp with a round window.

The number of degrees the hyperphoria lever moves is almost exactly half the number of degrees of the vertical displacement of the images. It is not exactly half, however, because the circumference which measures the angle made by the moving image, has for a center a point a little in front of the eye. (Fig. 3, *C*). But at a distance of 20 feet this error is not appreciable, and even if it were the dial could be graduated empirically. The closer the mirrors are together and the nearer the eye is held to them the less is the error. For the near point, however, the error becomes considerable, and if it is desired to test hyperphoria for the near point a special scale is necessary.

In a theoretically more perfect instrument, it would be necessary to have both the lateral and vertical movements produced by the lower mirrors. This would entail, however, a more complicated mechanism, and I think it is hardly demanded. In this model only one of the upper mirrors is moved. It would be better, however, to have them so arranged that they would move equally but in opposite directions. This is so, because if the lower mirrors be tilted for a high degree of lateral displacement, the moving of one upper mirror would produce a movement of the image along an oblique line instead of a vertical one and hence diminish or increase the reading. This error is very slight, however, and diminishes directly with the amount of lateral displacement.

The center of the curve along which the lateral movement of each image is made, is, for practical purposes, at the intersection of the line of sight with the axis of the lower mirror. Since the eye is a short distance behind this point, the lateral movement for near objects is perceptibly less than that registered by the instrument. It is thus necessary to make a scale for the near point and on this model I have done so, taking as the near point an object whose image is 30 cm. from the eye. The method of obtaining the scale must be modified from that adopted for the 20 ft. scale, since the image is about as far back of the real object as the distance between the upper and lower mirrors. The difficulty is overcome by having an upright line at this distance behind the object and in making the scale the image is adjusted with regard to this line and not with regard to the object.

The range of this model is from 10 degrees of exophoria to 15 degrees of esophoria. If additional range is required all that is necessary is to add prisms to the cells at the back provided for the purpose. Thus if a 5-degree prism, base out, were added before each eye, the range obtained would be from 0 degrees to 25 degrees esophoria, and if base in, from 5 degrees esophoria to 20 degrees exophoria.

There may be some objections raised to the use of the thread in this instrument. I must admit that it does seem rather reckless to have the accuracy of the instrument hang by a thread, as it were, but the little likelihood of the thread being broken and the ease with which a new thread can be inserted and the instrument readjusted, I think fully warrant its use. Other mechanisms could be devised for the purpose, but I think they would not increase the accuracy of the instrument to any extent.

The advantages of the instrument are obvious. Even without the use of the shutter mechanism it has the same advantage that Stevens' phorometer has over the ordinary prism test. This lies in the evenness and rapidity with which the reading may be obtained. In Stevens' phorometer, it is necessary to separate the images primarily at a distance equal to the limit of the instrument, that is about 10 degrees, and they are farthest apart when the heterophoria is least, and therefore most difficult to estimate. I think this is a decided disadvantage, for one image is on the fovea while the other is on a less sensitive portion of the retina, and it is consequently not only more difficult for the patient to estimate their relative positions, but he is likely to overlook or suppress one image entirely. In the reflecting phorometer, on the other hand, the images need be separated only so far as to produce constant diplopia.

Moreover, such difficulties are entirely overcome by the use of the shutter previously described. By means of this it is possible to locate the images upon corresponding points, in fact upon the foveas of both eyes. The very slightest heterophoria is thus detected at once, the image apparently moving in one direction or another, and when the apparent movement is overcome by moving the levers, not only the esophoria or exophoria is indicated on the scale, but the amount of hyperphoria as well. I have not tested the instrument with cases of amblyopia, but it is extremely likely that it will prove of the greatest value in just such cases, since the patient is seeing with only one eye at a time and hence has little tendency to suppress either image.

In testing the strength, or really the combining power, of the eye muscles, the instrument has very decided advantages. Ordinarily in testing the combining power of the muscles, first one prism and then another is placed before the patient's eyes until a strength is reached which the patient cannot overcome and diplopia is produced. The objection to this method is that the patient is tired out by having to overcome prisms so many successive times, and one can never be sure that he is not suppressing one image. With this instrument, however, separation of the images is gradually, though quickly, produced by the proper lever, and when the patient says the images are slipping apart the result is read off on the scale. This occupies no more time that it takes to read it.

Another very important use to which the instrument can be put is to give gymnastic exercise to the eye muscles. By moving the lever, the patient himself can do this, not by jerks as with prisms, but smoothly, and I find that it is possible for the eye muscles to abduct, adduct, or sursumduct to a greater extent than with prisms and that it is not so fatiguing to the eyes. By the use of this instrument I have no doubt that exercise of the muscles of the eyes will produce more satisfactory results than have hitherto been generally claimed for it.

I wish to express my great obligations to Mr. R. F. Rand for the very careful drawings he has made for me, and to Dr. James Bordley, Jr., for looking over the literature. So far as he has gone, Dr. Bordley has found no mention of any instrument at all similar to this one.

During a discussion following the reading of the above paper before the Maryland Ophthalmological and Otological Society, my attention was called by Dr. Hiram Woods to an article by Dr. Alexander Duane in the New York Medical Journal for August 3rd, 1889. In this article Dr. Duane describes a test for the insufficiencies of the ocular muscles that he calls the parallax test. The principle of this test, I find, is undoubtedly the same as that involved in the shutter test as described by me. "It consists of shifting the screen from one eye to the other and making the patient observe if the image moves, and if so, in what direction." Dr. Duane measures the amount of insufficiency by determining the prism required to overcome the movement in any one direction, and he claims that the test is an extremely delicate one, especially for hyperphoria. Dr. Duane evidently shifted the screen by hand, and it seems to me that if he obtained such excellent results in this rough way, the test, used in connection with the reflecting phorometer in the way I have described, should prove of still more value.

I have given personal instructions regarding points necessary to the manufacture of the instruments to E. B. Meyrowitz, of New York, from whom in future they can be obtained.

Discussion.

Dr. Theobald.—I think Mr. Verhoeff has devised an instrument that is going to be of distinct value and one having decided practical merits. The shutter device, so far as I know, is entirely novel and very ingenious, and accomplishes exactly what is aimed at. The instrument combines with the qualities of the Stevens' phorometer the power to determine the ability of the muscles to fuse images; in other words, it gives the strength of the muscles in overcoming diplopia. At the same time it is simple and not likely to get out of order. I at first made the criticism that if one of its strings should be broken it would be difficult to get the instrument gauged again, but Mr. Verhoeff promptly threw it out of gear and in a few moments had it rearranged, showing that objection was not well founded.

I congratulate him upon having done such an excellent piece of work, and I think the oculists will consider it an instrument of great practical value.

ON THE SOLUTION OF MERCURY IN THE BODY.

By Arthur Smith Chittenden.

(*From the Pharmacological Laboratory of Johns Hopkins University.*)

The apparently ready absorption of metallic mercury and its subsequent elimination in a soluble form has led numerous investigators to inquire into the action of the body juices upon the apparently insoluble metal.

That inunctions of finely divided mercury or the inhalation of the vapor can give rise to marked symptoms of mercurial poisoning has long been a matter of common knowledge. That this fact involves somewhere and somehow a solution of the metal is obvious; and the determination of the place and nature of this solution has held the attention of many investigators.

For some time it was supposed that the blood exercised an oxidizing influence on the metal; and although this belief obtains substantially to-day among pharmacologists, yet the experiments which first led to this view have long been considered fallacious. For purposes of investigation the method of introducing mercury into the blood usually consisted in anointing either abraded or vesicated surfaces with quantities of mercurial ointment; animals were also compelled to inhale mercurial vapor. As a result of these experiments, soluble mercury was found in the blood, urine, and fæces, and apparently, also in the form of metallic globules, in the depth of the epithelium and in the dejecta.

Oberbeck* in a series of painstaking experiments found, upon making microscopic sections of the area treated with mercurial ointment, that the corium was infiltrated with minute globules of the metal. After a similar inunction of vesicated surfaces, Zuelzer* found the ducts of sebaceous glands as well as the sheaths of the hair follicles filled with the metallic globules.

In a paper some years previous to the foregoing, Hoffmann† obtained precisely opposite results in a series of similar experiments. It remained for Rindfleisch‡ to repeat these investigations and to determine the reason of the discrepancy in results.

After anointing an unabraded surface and cutting sections as described, he found that if he sectioned with the blade passing through the deeper tissues first and out through the skin, no globules of metal appeared in the corium and deeper structures; whereas, if he reversed the block and cut through the skin first, the mercury droplets could be made out in the depths of the tissue. In other words, the metal was carried into the tissues mechanically in sectioning.

In the experiments in which inunction on abraded surfaces was practiced and in which the insoluble metal was found in the internal organs, the lymphatic spaces and the capillaries were·

* Oberbeck, Mercur. u. Syphilis. Berlin, 1861.

* Wein. Medicinal Halle, 1864.

† Hoffmann, Inaug. Diss. Würzburg, 1854.

‡ Rindfleisch, Arch. f. Dermat. u. Syph., 1870.

doubtless opened and the metal was picked up by the circulation.

The appearance of metallic globules in the fæces of dogs which have been anointed with mercurial ointment may also be explained by the fact that unless the ears alone be treated, it is almost impossible to prevent the animal from licking off and swallowing the mercury.

According to Hermann,* generally speaking, metallic mercury cannot as such pass through the intact epithelium in any part of the body. This is true of the respiratory epithelium as well as of any other. In cases where the mercurial vapor is inhaled, the metal is found condensed upon the surface of the epithelium, no globules passing beneath the surface unless they enter by some break in its continuity. Still other investigators, such as Hoffmann, Röhrig, Bärensprung, Neumann and Fleischer concur in this opinion.

If, then, in inhalation and inunction experiments insoluble mercury does not pass through the intact skin to be acted upon by the circulating fluids of the body, but does appear in soluble form in the blood and dejecta, what are the factors effecting solution? They may be found in two situations: in the secretions on the surface and in the menstruum of the ointment. That the secretions of the skin contain materials which will effect the solution of mercury has been sufficiently proven. Lewald has shown that by treating mercury with ammonium butyrate, a component of the secretion of the skin, solution follows; moreover, the sebaceous secretion contains various other agents capable of acting in this way.

When mercury is precipitated on the respiratory epithelium in inhalation experiments, Hermann† says that, aside from the oxidation processes which might be effected by the air in passing over these surfaces, we must suppose some supplementary oxidation as a result of the activities of the tissue juices. This is borne out by the researches of Rindfleisch‡ wherein he finds, after introducing blue ointment into the conjunctival sac and suturing the eyelids, that, although inflammation has occurred and pus has formed, subsequent section of the eye in glycerine fails to reveal any metallic globules.

The questionable methods of experimentation and the wide discrepancy in the results of investigation lead Schmiedeberg§ to cast serious doubt upon the power of the blood to oxidize mercury.

The possibility that the various investigators referred to may have unwittingly introduced soluble mercury and therefore obtained positive results is apparent, and it was with this contingency in mind that Fürbringer‖ devised a method calculated to eliminate experimental errors.

Having rubbed up definite amounts of mercury with gum arabic and glycerine, he obtained a dark-gray emulsion from which the larger globules separated out on standing; the remaining globules were exceedingly fine and remained in suspension. In the supernatant liquid Fürbringer found only very minute amounts of mercury; this emulsion he injected into the femoral veins of dogs. After a definite time, varying from twelve hours to seven days, he drew off and immediately defibrinated the blood. Having allowed the blood to stand until the corpuscles had settled to the bottom, the serum was decanted off and the organic matter destroyed by oxidation with HCl and $KClO_3$; the resulting solution was then submitted to electrolysis and positive evidence obtained in a number of experiments of the presence of soluble mercury.

In five experiments in which the animals were killed respectively, one, two, three, five and six days after injections, the chemical manipulations afforded plain evidence of the presence of mercury in the form of mercuric iodide rings. In four experiments no mercuric iodide whatever could be detected, and in three further instances the presence of mercury was questionable, as it could not be asserted positively that mercuric iodide was obtained.

Fürbringer's work is open to criticism in two particulars. In the first place, it is possible that a soluble compound is formed when mercury is rubbed in a mortar with solutions of gum arabic. Here, certainly, we have an exposure of finely divided mercury to oxygen, organic substances and to salts of potassium, calcium and magnesium. That it is possible for a soluble compound to be formed under these circumstances, Fürbringer admits; for, when his emulsions were allowed to stand for a long time in loosely stoppered vessels, a soluble mercurial compound, presumably mercurous mucate, was obtained. This possibility is further strengthened by the experiments of many investigators which show that when mercury is shaken with fluids containing salts and proteids a small amount of a soluble mercurial salt is formed.

A second criticism is that, oxidation of blood serum with HCl and $KClO_3$ will make soluble any metallic mercury which may be in suspension in the serum.

In justice to Fürbringer it must, however, be stated that he attempted by means of control experiments to show that he had not introduced soluble mercury into his animals and that the operation of defibrinating the blood and the subsequent chemical manipulations could not account for the mercury found in those of his experiments which yielded positive results.

Bearing in mind the criticism made upon previous investigations of this character, it is the object of this paper to present a method which shall, in so far as may be, eliminate questionable details of experimentation.

I have chosen the urine and fæces as the objects of investigation because they seemed to present the least possibilities of error; in so doing, the dangers of oxidation and contamination of the mercury by salts and fatty acids of the skin are avoided.

Method of Preparing and Injecting the Mercury.

An alcoholic solution of mercuric chloride was treated with stannous chloride until all the mercury was precipitated in a finely divided form; this was filtered and washed with hot water until the filtrate gave no precipitate with silver chloride. The residue on the filter paper was then suspended in a physi-

* Hermann, Toxikologie, Berlin, 1874. Also Harnack, Arzneimittellehre. Leipzig, 1883.

† Loc. cit. Also Harnack, loc. cit.

‡ Loc. cit.

§ Schmiedeberg, Arzneimittellehre, Leipzig, 1895.

‖ Fürbringer, Virch. Arch., 1880, Bd. 62.

ological salt solution; when examined under the microscope this suspension showed the presence of globules of mercury which were smaller than a red-blood corpuscle.

Having dissected out the femoral artery and clamped it centrally, about 5 ccm. of this suspension, containing approximately 0.25 g. of metallic mercury, was injected peripherally into the artery of each of four dogs.

The needle was withdrawn and in each case the clamp removed and the wound closed by deep and subcutaneous sutures. By thus deeply burying the artery the possibility of hemorrhage or of the animal licking up mercury was obviated. The urine and fæces of these animals were collected for a period of six weeks after the injection and analyzed for mercury.

Method of Detecting the Mercury in the Urine and Fæces.

For the method of detecting and determining the mercury in the urine and fæces I am indebted to Winternitz* I constructed a system of three upright glass tubes each of which connected with a common T-tube and contained a roll of pure copper gauze 20 cm. in length. The urine was collected from time to time, filtered, acidulated to 1 per cent. with HCl and passed over the copper rolls through the uppermost arm of the T-tubes.

Each day's urine passed through this system six times and the collecting was continued for six weeks. The rolls of copper gauze were then withdrawn from the tubing, washed with water, alcohol and ether and submitted to a high temperature in the combustion furnace for one hour.

In glowing the copper rolls, a bayonet tube was used which contained beyond the rolls of gauze a layer of copper oxide and a spiral of silver wire separated by suitable asbestos plugs. In the straight end of the tube which projected from the furnace a small bulb was blown and in this were placed leaves of gold foil.

During the heating a stream of dry carbon dioxide was passed continuously through the tube from the bayonet extremity; at the end of an hour a large number of minute globules of mercury could be clearly seen on the sides of the tube as it projected from the furnace and in the bulb; also an amalgam had formed upon the gold foil. These globules could be rolled together into larger ones and gave red crystals of mercuric iodide when subjected to vapors of iodine.

To determine the mercury in the collected fæces, these were extracted for several days with water, the filtrate acidulated and passed over another series of copper rolls; the heating of the rolls was then carried out as in the urinary determination but failed to reveal any mercury in the form of visible globules. When, however, the tube and bulb were subjected to iodine vapor, plain evidence of a ring of mercuric iodide was obtained. The amount of soluble mercury present in the fæces was very minute as compared with that in the urine. This is hardly contrary to what might be expected, since secretion of mercury in the bile is slow† and the reabsorption in the intestine is rapid.* Furthermore, my method would not detect the mercury present in the fæces in the form of a sulphide. The total amount of mercury injected into the four animals was approximately one gramme; the amount recovered from the urine was estimated to be about 20 mg. That the amount recovered should be small is borne out by the researches of Lewin† who finds that after inunctions with blue ointment, mercury continues to appear in the urine for eight months.

The finely divided mercury used in these experiments was freshly prepared for each animal in order to eliminate any possibility of oxidation on standing.

That finely divided mercury could have been excreted as such by the epithelium of the urinary tubules would hardly seem probable inasmuch as repeated microscopical examination failed to reveal the presence of any globules either in the lumen or in the epithelial cells themselves.

Fürbringer speaks of the formation of thrombi during his experiments at the point where the cannula was introduced into the vein; other observers have mentioned emboli in the lungs. By injecting into the femoral artery it was sought to have the emboli form peripheral wards. Having killed one of the animals used in the experiments, I examined microscopic sections of the paw of the leg injected and failed to find any emboli. When Prof. W. H. Welch examined sections of the lymph glands which were submitted to him he made the following interesting observation: Scattered among the lymphoid cells were numerous large multinuclear megalokaryocytes, a condition resulting from parenchymatous‡ embolism of the bone marrow; these cells are subsequently expelled into the circulation from which they are filtered out by the lymphoid tissue.

The appearance of these cells in the lungs has also been observed in animals in which embolism of the bones had been produced.

Just how the solution of mercury by the body juices is effected and what part is played by the albuminous constituents, we cannot say, but that solution is effected and the mercury eliminated as an albuminate§ seems to be true.

Van der Does‖ finds that after shaking dilute egg albumen with finely-divided silver and then filtering, the filtrate is no longer coagulable by heat; the albumen thus treated will not decompose when exposed to air, and that silver has gone into solution. Albumen treated in this manner with mercury does not give a similar result.

* Winternitz, Arch. f. Exp. Path. u. Pharm., Bd. 25, p. 225.

† Lewin, Toxikologie II Auf., 1897, p. 116.

* Real encylopädie des gesammten Heilkunde, Bd. XVI, p. 317.

† Lewin, loc. cit.

‡ Lubarsch, Fortschr. d. Med., 1893, II, p. 805. Maximow, Virch. Arch., 1898, CLI., p. 297.

§ Real encylopädie der Gesammten Heilkunde, loc. cit.

‖ Hoppe-Seyler's Zeitschrift f. Physiol. Chemie, XXIV, p. 351.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

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PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Monday, January 9, 1899.

Exhibition of Medical Cases.—Dr. Futcher.

During the fall of 1898, Lancereaux, of Paris, published a new method of treating aneurisms. He published the first communication, in connection with Paulesco, about the 1st of October and the method is as follows:

He injects into the subcutaneous tissue of the thigh 250 cc. of a 2 per cent. solution of gelatin in normal salt solution. Of course, it is thoroughly sterilized and injections are made with aseptic precautions. The injections should always be made at a considerable distance from the aneurism, and he considers the most satisfactory place to be the subcutaneous tissue of the thigh. The interval between injections should be from two to fifteen days. He states that about 20 injections are necessary to produce a cure, and from a considerable series of cases in which he has adopted this treatment quite a large percentage are reported as cured. He finds, however, that ordinary diffuse dilatations of the arch of the aorta are not relieved by the treatment, but that the most satisfactory cases are the saccular dilatations of the aorta, or of any of the other vessels.

Huchard, also, used this method of treatment, but recommends that a weaker solution than the 2 per cent. be used. He found that after the injections were given a great deal of pain was complained of for several hours at the seat of injection, so he recommends the use of a 1 per cent. solution, which apparently causes no pain. He reported two cases in which death occurred; one was a case of pulmonary tuberculosis, in which he believed the hæmoptysis was due to minute aneurisms on the small vessels crossing the pulmonary excavations. This patient died rather suddenly during the treatment. The second case was one under the care of Dr. Barth, and, in this instance, the patient after the sixth injection had a sudden attack of dyspnœa, suffocation, and died in a few minutes. An autopsy showed definite clotting in the aneurismal sac; there was a layer of fibrin about 4 cm. thick all over the wall of the sac, but the clots had extended into all the vessels, excepting the left subclavian, springing from the arch of the aorta, completely occluding them, and causing sudden death.

The beneficial effect of the treatment is supposed to be due to increased coagulability of the blood. Intra-peritoneal injections have been made in the rabbit by Lancereaux, and he believed that the coagulability of the blood was always increased. However, the adoption of this mode of treatment of aneurism has led to a great deal of discussion before the Academy of Medicine, in Paris, and various observers claim that the coagulability of the blood is not increased. Laborde claims that it is not, and says that gelatin is not absorbed when injected into the peritoneal cavity, and that he has found the same amount of gelatin several hours after injection, as was originally given. He states that possibly eventually it may be absorbed, and if so, it is because it undergoes peptonization. Laborde recommends that the gelatin injections be made into the sac itself. Camus and Gley have performed experiments and found that there is no increase in the coagulability of the blood after intra-peritoneal injections of gelatin in rabbits—that is, there is no diminution in the time required for coagulation to take place.

We have now tried the treatment in four cases of aneurism in the medical wards of the Johns Hopkins Hospital.

The first was that of J. B., who was admitted about two months ago, with a definite saccular aneurism of the arch of the aorta about the junction of the transverse and descending portions of the arch, at least that is where we believed it to be during life. He had received six injections—two of the 2 per cent. solution, and four of the 1 per cent., because it was found that the first gave considerable pain. This pain was very intense and most severe about six hours after the injection. The patient appeared to be doing fairly well, when he was suddenly seized with an attack of dyspnœa, coughing and profuse hemorrhage, and died. At the autopsy there was found a general dilatation of the arch of the aorta with a localized saccular dilatation about the junction of the transverse and descending portion of the arch. At the point of pressure of the sac on the left bronchus there had been a perforation causing hemorrhage and death. There was no deposition of fibrin on the sac wall.

The second case in which the treatment was adopted was a patient, U. C., with aneurism of the descending portion of the thoracic aorta. He has now had 28 injections, more than the number supposed to be required to produce a cure. There was definite pulsation visible and palpable over the lower part of the thorax with a definite diastolic and systolic murmur in the back. There was intense pain at the seat of pulsation previous to the adoption of this treatment. Since the treatment was begun he has had very marked diminution in the amount of pain, and the pulsation is appreciably diminished. During the time of treatment he has gained 19 pounds in weight. It is the most satisfactory case we have had, so far, out of the four.

The third case is that of O. G., who has a saccular abdominal aneurism. He has now had 16 injections, with little or no evident improvement. He still has a great deal of pain.

The fourth case, C. L., has had 21 injections for a rather diffuse dilatation of the arch of the aorta. In this case, and in that of U. C. and O. G., there has been a marked increase in the coagulability of the blood after each injection—that is, the time of coagulation was distinctly diminished. (Exhibiting cases.)

An interesting condition that has followed the injections in Case IV is the occurrence of localized tumors at the seat of infection in the abdominal wall. The injections were made here because we thought there might be less pain than that which followed injections in the thigh. The pain was not, however, much diminished. The day following the injection a nodule the size of a hickory-nut frequently developed, occasionally accompanied with an elevation of temperature. These nodules persist for eight or ten days and then gradually disappear.

In the second case the coagulation time averaged about three minutes for the first ten injections and afterwards became

much delayed, for a short period, requiring 17 minutes for coagulation to take place. What the explanation of this is I cannot say, for it has again come down to five minutes.

THE SCHOTT TREATMENT OF HEART DISEASE.

About two years ago Dr. Camac read a paper before this society describing fully this method of treatment. Last summer I had the opportunity, through the courtesy of Dr. Theodore Schott, of seeing the method as used at Bad Nauheim. The treatment consists of two factors: the giving of thermal saline and carbon dioxide baths and the use of carefully regulated muscular exercises. The constituents of the saline bath consist largely of sodium and calcium chloride and the temperature is about 93 degrees F. After a series of these baths the patient is given a series of the carbon dioxide baths. The effect of the bath treatment is believed to be due to a stimulation of the peripheral circulation, thus increasing the amount of blood in the skin and subcutaneous tissue and in this way relieving the heart.

The exercises are believed to have practically the same effect; the patients usually get the baths in the morning and the exercises in the afternoon. The baths are given first for about six minutes and the time gradually increased until the patients are allowed to remain in the bath for about eighteen minutes.

I saw a patient given his first bath. It was a case of myocarditis in which the heart was very large, much dilated and its action extremely weak. Before putting him in the bath the area of cardiac dullness was carefully mapped out on a piece of transparent paper, and after the bath the cardiac dullness was again percussed out, the first diagram was placed over the second by means of definitely located points and any change in the area of cardiac dullness was thus noted. It was remarkable in this case to see the change; there was fully a finger's breadth difference in the extent of dullness before and after the bath.

At first the diminution after the bath is not permanent, but eventually a gradual gain is made and a widely dilated heart may diminish to practically its normal size.

Efforts have been made to devise a means of giving these Schott baths in hospitals and other institutions, and Theodore Schott has given formulas according to which the various baths can be prepared and carbon dioxide generated. The usual method of preparing the latter has been to use hydrochloric acid and sodium bicarbonate. During the past year a firm in New York known as The Triton Company have devised a means of dispensing with the use of hydrochloric acid and recommend a simpler way of generating the gas. They have prepared boxes containing a package of sodium bicarbonate and cakes of sodium bi-sulphate, the gas being generated by the action of these two salts upon each other. In addition to the bicarbonate of soda five pounds of salt and varying quantities of calcium chloride should be first added to forty gallons of water in the bath. The sodium bicarbonate is then put into the water and the cakes of sodium bi-sulphate, of which there are eight, are placed about the patient as follows: Two beneath the shoulders, two at each side of the body, and two under the knees. In two or three minutes there is a rapid generation of the gas and the patient may then be placed in the bath, where he remains a variable time, according to the stage of the treatment.

This patient with myocarditis has received the treatment here. He has had no rheumatism; has not been a heavy smoker, but a rather hard drinker, and it was found on physical examination that he had a much dilated heart, the point of maximum impulse being in the sixth interspace 12 cm. from the mid-sternal line, just before the first saline bath was given. His heart's action was very weak, the pulse very feeble and many of the beats not recorded at the radial pulse. Dr. Hastings was kind enough to make these charts, on which the red lines indicate the area of relative cardiac dullness before the bath, and the dotted lines that after the bath. The greatest width of relative cardiac dullness before the first bath was 12 cm., and after the bath 9 cm. With each succeeding bath the area of dullness gradually diminished and this chart represents the present area of relative cardiac dullness, which you see is markedly diminished. The apex beat is now in the 5th interspace 7.5 cm. outside the median line and the greatest breadth of relative cardiac dullness is only 7 cm. His condition is much improved and he goes about the wards with very little dyspnœa.

Dr. WELCH.—Referring to the first cases, I should like to ask whether in the gelatin treatment for aneurism any attention has been paid to factors other than the coagulation time, particularly as to whether there is any increase in the number of platelets in the blood or any diminution in the red-blood corpuscles? I speak of this because the coagula in aneurism are not ordinary clots as they form outside of the body, but are genuine thrombi which consist in their inception of platelets, and it is difficult to bring the occurrence of these thrombi in the body into any definite relationship with the rapidity of coagulation of the blood. Many diseases like lobar pneumonia and acute rheumatism in which there is increased fibrin content are not so frequently associated with peripheral thrombi as are typhoid fever and certain anæmic and cachectic conditions in which the fibrin content is low. We cannot bring the appearance of coagulation in the living vessels into direct parallelism with the coagulability of the blood as ordinarily understood. There are indications suggesting a connection of these thrombi with the number of platelets in the blood. In chlorosis, for instance, the number of platelets is increased and peripheral thrombosis is a well-recognized complication, whereas in pernicious anæmia the number of platelets is diminished and thrombosis rarely, if ever, occurs. In hæmophilia there is sometimes total absence of platelets. There is much for the view that the number of platelets is an index of lowered resistance of red corpuscles. If, therefore, there is any evidence that the gelatin treatment favors the production of thrombi in aneurisms, it seems to me that some light may be thrown upon the explanation of this occurrence by the study not only of coagulation time and fibrin content, but also of the possible influence of the gelatine injections upon the resistance and number of the red copuscles and the number of platelets.

Aneurism of Aorta, Compressing and Rupturing Into Left Bronchus.—Dr. Flexner.

Anatomical Diagnosis: Aneurism of the aorta, rupture into the left bronchus, hæmoptysis; aspiration of blood into the lungs; compression of left bronchus; slight bronchiectasis, and carnification of the lung; acute splenic tumor; slight chronic nephritis.

The pericardial sac does not contain an excess of fluid; both layers of the serous membrane are smooth. There projects into the summit of the sac a roundish tumor springing from the aorta, which is intimately united with the pulmonary artery. The heart was opened *in situ*. It was found that springing from the left lateral wall of the ascending portion of the aortic arch is a saccular aneurism projecting toward the left side. The projection into the pericardial sac is found to be due to an extension from this aneurism. The dilatation of the aorta begins 5½ cm. above the attachment of the aortic valves and, as will be seen, includes portions of the ascending, transverse and descending aorta. An opening which is approximately circular and measures 6½ cm. is situated on the left lateral side of the artery. This opening can be divided approximately into three segments; the first third springs from the ascending, the second from the transverse portion and the third, which is the shortest, from the descending portion of the arch. The depth of the sac is approximately 4 cm. The sac, as stated, extends to the left and pushes aside the upper lobe of the left lung to reach the pleural surface with which it is firmly united. Finally it comes to impinge on the left bronchus, and it has also grown together with the fibrous wall of this structure. The œsophagus also is pressed upon by that portion of the sac which has come to lie next it.

The entire main bronchus, from the bifurcation of the trachea to the first division in the hilus of the lung, is pressed upon by the sac of the aneurism. As a result the walls of the former are distinctly thinned and there is a marked lateral compression of the tube. The bronchus has been perforated just below bifurcation of the trachea at a point coinciding with the intercartilaginous tissue between the second and third rings. The mucous membrane covering the second ring is eroded, while that over the third is swollen and defective superficially. The membrane between the third and fourth rings is much attenuated and appears to be covered by nearly intact mucous membrane only. There are two small ruptures to be made out in this membrane, which might readily have been produced in the removal of the lungs and bronchi. The mucous membrane of the bronchus where it is freed from the recently coagulated blood which covers the surface is pale. The left lung is bound to the chest wall and to the pericardium and aneurism by old adhesions; the apex only is crepitant. The bronchi upon section show a moderate dilatation of the medium-sized tubes, while the lung substance is congested, dense and more or less airless, the consistence being increased. In this carnified and congested tissue there are scattered small whitish or grayish points, and from the surface a cloudy fluid can be expressed. Certain areas of the lungs present a grayish and slightly coal-pigmented aspect and are semi-translucent. The right lung is voluminous. There are moderate pleural adhesions, the anterior and superior half being bound to the pericardium. Where free from adhesions to the chest walls and pleura it shows blotches of hæmorrhage, and upon section there are present deep red areas corresponding to points of blood aspiration. The medium-sized bronchi are plugged with recent clots of blood. The trachea and larynx, except for the staining of mucosa, are free from coagula of blood.

The aorta is the seat of marked arterio-sclerosis with slight calcification. The sclerosis does not begin immediately above the valves in that it leaves the first part of the aorta clear for a distance of 5 cm.; the most marked sclerosis is in the transverse arch. The sclerosis is less marked again in the thoracic aorta and abdominal aorta where relatively few sclerotic patches occur. The sac of the aneurism is almost entirely free from clots; the coats of the artery are shown to be present everywhere, the inner coat presenting an irregular corrugated appearance. Fatty patches, a few elevated fibrous nodules and a number of calcified areas measuring several millimetres in diameter—these last showing a slaty pigmentation—occur in the sac of the aneurism. These slaty and calcified areas are, on section, found to agree with underlying and closely adherent, nearly black lymphatic glands. The coagula upon the wall consist merely of a recent granular deposit, not exceeding a millimetre in thickness and imperfectly covering the inner surface.

Bacteriological examination showed the lung, liver and kidneys to contain the bacillus lactis aerogenes. The lung and liver, spleen and kidneys gave the micrococcus lanceolatus. 0.3 cc. of a culture of the micrococcus injected into a mouse produced death from general septicæmia.

Miss Reed has kindly examined the sections from the case, the chief interest of which centres in the spleen and the left lung. The spleen shows in its substance, especially in the neighborhood of the capsule over the ventral surface, a number of hæmorrhages, some small and others larger, although the largest does not exceed 1 or 2 mm. in diameter. In a broad way two kinds of hæmorrhages may be distinguished, although the line of demarcation is not absolutely sharp. The larger ones consist of red-blood corpuscles chiefly, with probably a due proportion only, of white corpuscles; the smaller, infiltrating areas which may not certainly be hæmorrhages, but localized congested areas, show a less perfect preservation of the hæmoglobin and the number of leucocytes with irregular nuclei considerably increased. Among the leucocytes in these latter situations are cells, the protoplasm of which reacts in a manner peculiar to hæmoglobin, which contain single nuclei or nuclei undergoing fragmentation. Similar cells to these are found distributed throughout the pulp of the spleen and are probably relatively as numerous as in the congested or hæmorrhagic areas just mentioned. Sections stained by the Biondi-Heidenhain method seem to prove what those stained in methylene-blue and eosin indicated, that these cells are normoblasts. The contents of some of the larger branches of the splenic vein are red corpuscles, leucocytes, cells with spindle-shaped nuclei; the latter were not improbably endothelial cells, derived from the vessels, post mortem. Small thrombi consisting of platelets and of leucocytes are also found in dilated veins containing in addition red corpuscles and endothelial cells presumably desquamated. The mixture of leucocytes and

platelets form small islands within the lumen of the vessel. Capillary thrombi in the region of the small hæmorrhages were not discovered. In sections stained by Weigert's fibrin method this element occurs in foci in the splenic pulp. Finally, a fairly large number of cells containing red corpuscles are present in the pulp.

The description of the lung is limited to the left lung. The bronchi are moderately dilated and contain mucus, fragments of red corpuscles, and more or less modified desquamated cells. The blood-vessels in the wall are swollen and the wall is infiltrated throughout with round cells, some of which present exquisitely reticulated nuclei, placed somewhat eccentrically, and resembling plasma cells. This infiltration is not limited to the wall of the bronchus but involves the connective tissue which includes in the same sheath the vein and the artery. The artery shows a new growth of tissue in the intima, which is young and cellular and not annular, but is developed especially on the side of the vessel next the bronchus. The irregular distribution of the new tissue in the intima is shown in a section which includes a branch of the artery, for the new tissue is developed almost exclusively on the side of the vessel, next to the bronchus and is very little present in the point of origin of the new branches. In the lung the new growth of tissue is in the pleura—in the interlobular and perivascular tissues especially. The alveolar walls, it is true, do show an increase in the immediate neighborhood of the perivascular infiltration, but at distances from this there is only a filling up of the alveoli with desquamated epithelial cells, serum, a few leucocytes and a minimal amount of fibrin. The greatest amount of fibrin is in the immediate vicinity of the largest and most infiltrated bronchus. Not a few of the desquamated epithelial cells contain blood-pigment, or coal-pigment, or red-blood corpuscles. In sections stained in alkaline methylene-blue and eosin there were short chains of cocci to be made out. Thrombi are wanting in the vessels in this organ.

The type of liver cirrhosis is syphilitic. Sections through the coarse fibrous band in this organ showed a dense sclerotic tissue containing numerous islands of liver substance and a moderate number of newly formed bile ducts. Some blood-pigment and partial obliteration of the smaller-sized arteries through an annular growth of connective tissue in the intima are also present. Gummata as such are not present in any of the sections examined. The kidney showed a marked degree of parenchymatous degeneration and a small amount of new connective tissue. The heart muscle exhibited a marked degree of fragmentation and segmentation of the myocardium. The type of fragmentation is that regarded by Mr. MacCallum as being preceded by degeneration (sarcolytic) of the affected fibres.

Multiple Metastases from Pelvic Sarcoma.—[See BULLETIN for April, 1899.]

DR. FLEXNER.—The case reported by Drs. MacCallum and Harris is interesting from several standpoints. The distribution of the metastases exhibits two modes of dissemination of tumor cells: (1) Blood-vascular and (2) lymph-vascular. The nodules in the lungs undoubtedly owe their development to the first-mentioned mode. This is rendered probable not only by the relations of the primary and secondary tumors, but also from the fact that Dr. MacCallum succeeded in tracing the growth along the walls of the blood-vessels to the nodules situated especially in the pleura, and also found groups of tumor cells in blood-vessels in the lungs. The testicular growth is conceivably of blood-vascular origin, the tumor cells having passed through the lungs and gained access to the general circulation. I am, however, disposed to regard the invasion of the testes as having taken place through the lymphatics, from the pelvic growth, by means of retrograde transport—a phenomenon not so very infrequently met with under similar circumstances.

As Dr. Harris pointed out, the streptococcus in this instance was highly pathogenic, not only for human beings but also for mice, an observation that has interested us greatly, in that our experience has been that growths of streptococci from human autopsies do not usually exhibit striking pathogenicity for these small animals. The streptococcus infection in this case was doubtless an example of terminal infection. We have now encountered a number of instances of terminal bacterial infection in malignant tumors.

NOTES ON NEW BOOKS.

The American Year Book of Medicine and Surgery. Edited by GEORGE M. GOULD, M. D. (*W. B. Saunders, Philadelphia*, 1899.)

The standard of previous years has been kept up in this work. It contains 1032 pages of text and 70 pages of a complete index. In the preface Dr. Gould refers to the omission of the name of Dr. William Pepper from the list of contributors. His place has been taken by Dr. Stengel and Dr. Edsall. The editor draws attention to the increasing difficulty of the yearly task of selecting what articles shall be noted. In this connection the hope may again be expressed, that it might be possible to give the titles of the most important articles not referred to in the text. If space allowed this, it would be an addition to the value of the book. The extracts are well made and evidently combine a maximum of information in a minimum of space. Altogether Dr. Gould and his staff of editors are to be congratulated on the Year Book for 1898.

Annual and Analytical Cyclopædia of Practical Medicine. By CHARLES E. DE M. SAJOUS, M. D., and one hundred associate editors. Volume II. (*The F. A. Davis Co., Publishers, Philadelphia.*)

The second volume of this valuable cyclopædia covers the subjects from "Bromide of Ethyl to Diphtheria." It contains 607 pages of useful reading matter. The object of the editor has been not only to facilitate the labor of the practicing physician and to assist investigators and authors in their researches, but also to render clear, through contributions from men possessing special knowledge or unusual experience in a particular line, diseases which, owing to their complexity, are not generally understood. The high standard of work commenced in the first volume is here maintained. The second volume contains among others, excellent articles on "Cerebral Hemorrhage," by Dr. William Browning; "Cirrhosis of the Liver," by Professor Adami; "Cholera," by Professor Rubino; "Cholelithiasis," by Professor Graham; "Diabetes," by Professor Lépine; and "Diphtheria," by Drs. Northrup and Bovaird. The editor states in the preface, in reply to numerous inquiries, that he himself wrote the unsigned article on "Animal Extracts," which appeared in the first volume.

Manual of Physiology, with Practical Exercises. Third Edition. By G. N. Stewart, Ph. D., Professor Physiology, Western Reserve University. (*Philadelphia: W. B. Saunders*, 1898.)

The rapid appearance of successive editions of this conveniently sized manual is sufficient evidence of a continued demand among medical students for text-books of smaller compass than the well-known standard works.

The present author, unwilling to meet this demand with a more or less elementary account of the subject, succeeds in crowding into his books all its details and gains the desired reduction in size by conciseness and brevity of treatment. The book is accordingly replete with facts, and extremely suggestive to one who possesses a previous knowledge of the subject. But as the high degree of condensation is necessarily attended with a corresponding loss in clearness and intelligibility, it is at least questionable whether it is really suited to the needs of medical students.

The practical exercises which, at first glance, enhance the value of the book, occupy about one hundred pages out of a total of somewhat over eight hundred. But the conviction grows on one that the author might have utilized this space more profitably to the reader as well as himself, if it had been expended upon a fuller and more lucid exposition of the general text. The frequent cross references from text to exercises in itself seems an acknowledgment on the part of the author of the insufficiency of the former. After all, the exercises claim no special merit as far as the choice of experiments is concerned; quite a number of excellent laboratory manuals, such as Stirling's or Brodie's, amply provide for the students' needs in this direction, while their grouping under the several chapters with reference to the systematic course, to which the author calls attention in the preface, will hardly be expected to secure a similar arrangement *in practice*. That the latter is advantageous and desirable for many reasons goes without saying, but its actual attainment depends on more things than the position of the exercises in a manual.

The book otherwise possesses many admirable features. We need only mention the superior character of all that pertains to its mechanical make-up, the number and variety of its illustrations, and the extent to which the most recent advances in physiology have been appropriated and used throughout the volume. We are a little surprised to find in so crowded a book a long paragraph on the *Care of the teeth*, a sort of error in perspective which also crops out occasionally in passages in which a relatively unimportant point is spread over a number of pages, out of all proportion to its value and significance. The discussion of the "Rate of blood-flow" covers about nine pages while the "origin of urea" is disposed of in three pages. In the chapter on nutrition we also note the omission of Drechsel's theory of the formation of urea and the scanty treatment given to the inorganic compounds, some of which like Ca have lately acquired so much significance in the general economy of the body. A few minor errors, like the formula for uric acid on page 436, the reference to Fig. 143 on page 519, and the incorrect account of the Holmholtz arrangement of the induction coil should have been corrected in a revised edition.

G. P. D.

The Peritoneum. By Byron Robinson, B. S., M. D. Part I: Histology and Physiology. 4°. Number of pages 405 (not including a bibliography of 103 pages). 247 illustrations. (*Chicago: The W. T. Keener Co.*, 1897.)

This volume is the first of what the author evidently intends to be a series of books dealing completely with the subject of the peritoneum. He tells us that it "is the outcome of a half dozen years of personal labor in experiments in the peritoneum, in the study of its anatomy and in microscopical research. The labors of others have been consulted and credited." Indeed, so ready is the author to give credit to those who have aided him, he has often, we fear, ascribed to other investigators much that they would not claim as their own.

Dr. Robinson has been anxious to follow the example of the illustrious John Hunter, by distinguishing himself in scientific studies of value to medicine. He has put his whole soul into the work. It is dedicated to his wife and professional associate, Dr. Lucy Waite. Each chapter is headed by quotations from general literature which have appealed to the author as particularly fit. Wordsworth and Dryden, Gibbon and Froude, Lord Bacon and Emerson have all served to inspire the author in his work. The chapter on the blood-vessels, for instance, is headed by a quotation from Tennyson's Brook:

"Men may come and men may go, but I go on forever."

On the title-page the following is quoted from Schiller:

"To contro a subject, to be its master, to concentrate upon it all that is absolutely necessary, demands, in truth, the powers of a giant, and is more difficult than one would think."

Eager to discover the secrets of the structure of the peritoneum, Dr. Robinson has been led into attempting the mastery of many subjects necessary for this work, histology, histological technique, physiology, pathology, comparative anatomy and the history of medicine. The result has been most remarkable, as the extracts given below will show.

The book is divided into chapters. "Owing to an attempt to make each chapter as complete as possible," says the author in the preface, "repetitions have been to a certain extent unavoidable." Indeed, the author has been so desirous of expressing in every paragraph and sentence the totality of his knowledge of the subject, that repetition might be found on every page were Dr. Robinson capable of expressing his ideas so accurately that they would appear to be quite the same when they are the second time transcribed. The titles are the only clues as to the specific nature of the various chapters.

The absolute disregard of logical order displayed by the author is the most remarkable thing about the book. This is indicated in the extracts quoted, but to be fully enjoyed must be sought in the original.

"Diligence and accuracy are the only merits which an historical writer may ascribe to himself."—Gibbon, heads the historical sketch with which the book opens. In the first paragraph the time of Erasistratus is given as from 340-280 B. C.; in the second paragraph that of Galen is given as 131-201 to 210 A. D. Then the author goes on to say, "Galen must have been in the possession of the writings of Erasistratus, for he noted the fact in regard to the lacteals of kids 150 years after the death of Erasistratus." Further on in the book the following account is given of the origin of the cell doctrine and of its application to the study of the peritoneum. It will not seem strange to state that the organ known as the peritoneum is composed of simple cells, when one recognizes the penetrating power of the microscope and the vigorous and far-reaching investigations of the nineteenth century" (p. 26). After a considerable discussion of the work on the cell of Schleiden, Schwann, Muller and Johannes Miller, to each of the last two of whom is given in different parts of the same paragraph the credit of popularizing Schwann's works (Johannes Mueller is evidently meant), the author goes on to say: "At this period of the world appeared the immortal Bichat, whom the French claim founded histology, by employing the discoveries of Schleiden in the plant cells and those of Schwann in the animal cells" (p. 26). It will, perhaps, be remembered that Bichat died in 1802, two years before the birth of Schleiden, and eight years before the birth of Schwann.

What has confused the historian is the fact that Bichat called the peritoneum a "cellular membrane," meaning, thereby, one containing areolar connective tissue, which, at his time, was commonly called cellular tissue. For any understanding of our modern cell concepts, the use of the microscope is necessary.

Bichat, owing to the imperfections which existed in the instrument while he lived, put little faith in the value of the microscope as a means of tissue study. Considering the work done of recent years in cytology, it is not uninteresting to read the concluding remarks of Dr. Robinson on this subject: "Finally, the last break in traditional thought was made by the celebrated Brecke, who stated that a nucleus was not necessary to any cell. We now have the final definition of a cell—that is, a mass of protoplasm" (p. 27). Brücke is here probably referred to. Brücke is celebrated for having been the first to suggest definitely ('61) the modern conception of ultra-cellular units ranking between the molecule and the cell.

"The peritoneal membrane," he tells us, "is not dissimilar to the skin, being of about equal area" (p. 14). In the discussion of the various elements composing the peritoneum, he tells us "Perhaps the most typical specimen to observe a connective tissue corpuscle is in the blood-vessel wall of the broad ligament of a gestating turtle." Among elements not before described, is the "elastic tissue cell." "The elastic cell is what gives to the peritoneum its peculiar quality of adaptation to environments. The elastic cell must belong to a certain extent to the endothelia, for which they are capable of extension and contraction to a wide degree. The elastic fibre, composed, of course, of cells, is produced, according to Ranvier, by fusion of small globules. The elastic cell is very abundant; it is associated with the genital organs and endows them with the wonderful power of changing their conditions and of returning to normal without loss of integrity" (p. 31-32).

Here we have a most curious example of the confusion of ideas of form and function, so characteristic of the author. He has evidently fused an idea of the elasticity of the endothelial cells, and an idea of the existence in the peritoneum of elastic fibres into the vague conception of elastic cells.

We have not space at our disposal to quote here at greater length the author's original descriptions of his anatomical findings.

As to the physiology, "especially will we be surprised to know that the peritoneum of the dead animal will absorb, for many hours after death, exactly similar to that of the living" (p. 35). "The physiology of the peritoneum must be looked for in the inter-endothelial space by its dilatation and contraction. The cover-plates are, perhaps, not *engaged much in physiology* (sic). The hard, indurated metamorphized protoplasm of the cover-plate aids chiefly in a mechanical way to facilitate motion, when aided by the visceral fluid secreted through the inter-endothelial space. However, the cover-plate doubtless plays a rôle in osmosis. "The forces which are said to induce peritoneal absorption of fluids may be enumerated as follows: (*a*) Vital cell forces; (*b*) stomata; (*c*) imbibition; (*d*) filtration; (*e*) intra-abdominal mechanical pressure; (*f*) osmosis" (p. 394). "Through ages of evolutionary processes of infective invasion, the pelvic, appendicular and gall-bladder region (the region of the large intestine) has acquired a physiology which resists the infectious germs in the common regions of peritonitis" (p. 399).

Although the object of the present volume is to deal mainly with the normal histology and physiology of the peritoneum, the author does not hesitate to refer to his extensive clinical and pathological experience when this may aid in making clear his thought. "The peritoneal surface is equal in area to the skin, and when injured by traumatic processes or attacked by disease, shows similar effects, as profound shock, significant vascular disturbances and depressions. A square foot of peritoneum being inflamed shows similar disturbances as the inflammation of a square foot of skin. In the peritoneum the inflammation is not so apt to be circumscribed or limited as it is in the skin, and hence the more danger of sepsis. Sepsis may pass through the peritoneum and leave it, as a bullet leaves a gun-barrel, uninjured" (pp. 256-257). "When foreign bodies (microbes or colored granules) enter the peritoneum the leucocytes swarm out (*a*) to digest the invader, (*b*) to surround or imprison the microbe or (*c*) to sterilize the germ" (p. 289).

Of equal value are the author's researches in the comparative anatomy of the peritoneum. "In this work we have examined the peritoneum of man, horse, dog, sheep, cat, cow, pig, hen, woodpecker, shypoke, frog, turtle, rabbit, crawfish, dove, guinea-pig, rat, fish, and embryos of man and some other animals. The material has been ample, but it would have been desirable to examine the peritoneum of monkeys and other animals only obtainable by living in proximity to a menagerie, where one could examine systematically the various genera and species and note the differences. However, material has been sufficient to induce me to believe that the peritoneum of vertebrates is constructed so much alike that it is equally well to select two animals, as the rabbit and the frog (cheap and conveniently obtainable), and carefully interpret the phenomena of structures and function of their peritoneum. The endothelia of the fish are like those of mammals. The crawfish has relatively small-sized endothelia, and they are very compact" (p. 34). "This work has proved that the structure of the peritoneum of vertebrates and mammals is quite similar" (p. 23). "The turtle (amphibia, *sic*) is one of the best animals to show vast interstitial subperitoneal spaces" (p. 395).

Many of the illustrations taken from the literature, especially those from Kolossow's articles, are well reproduced. The great number of the drawings, made by the author himself, serve to adorn the text. The bibliography is as complete a one as money can buy.

Taking the book as a whole, it reminds us more strongly of the remarkable Syllabus of Ephraim Cutter on Clinical Morphologies, than any other book that we have seen, though the latter has the additional merit of better order and of much greater condensation. It may be remembered that Cutter names among other things in a long list of objects to be looked for when examining the sputum, the "lumina of blood-vessels," and apologizes for not adding to the list the difficult "morphology of the air." B.

The American Pocket Medical Dictionary. Edited by W. A. Newman Dorland, A. M., M. D. Containing the Pronunciation and Definition of over 26,000 of the terms used in medicine and the kindred sciences, along with over 60 extensive tables. (*Philadelphia: W. B. Saunders*, 1898.)

This is a handy little volume that, upon examination, seems to fairly fulfill the promise of its title, and to contain a vast amount of information in a very small space. It must be, of necessity, incomplete; but it is somewhat surprising that it contains so many of the rarer terms used in medicine as it does.

The principal criticism suggested, and this seems a little ungracious when so much is given in so small a compass, is that it might well have contained a few more of the modern synonyms of the nervous system, proposed by Dr. Wilder, than we find in it. These terms have already been employed in medical literature and are likely to be employed again, and their inclusion would have added to the value of the book.

The work is of rather convenient size, and is attractively gotten up.

Hay Fever and its Successful Treatment. By W. C. Hallopeter, A. M., M. D. (*Philadelphia: P. Blakiston, Son & Co.*, 1898.)

About two-thirds of this little volume is taken up with the history of hay fever, or, what amounts to the same thing, the discussion of its exciting and predisposing causes. Then come descriptions of the symptoms and theories of its pathology, etc., and about ten pages at the end of the work are devoted to the treatment. The author pins his faith upon a systematic course of daily atomizing, and swabbing the nasal and post-nasal mucosa with antiseptic solutions (Dobell's solution, well diluted, is recommended), with such general tonic measures and attention to the diet, habits, etc., as appear indicated in each individual case. Any existing

abnormal condition of the nasal passages is, of course, to be looked for and remedied if possible. In old cases, when the nerve habit of this disease has become established, he advises this treatment for several weeks before the expected onset of the attack, but does not apparently give the duration of the treatment, and it may be assumed that in some cases, at least, he would continue it through the whole hay fever period. It is to be inferred that by this method also, and indeed he expressly so states in his remarks on prognosis, he succeeds in time in breaking up the tendency and curing the patients in the majority of cases.

The book is clearly written and can be read comfortably at a sitting. A bibliography is appended that seems fairly full as regards recent American contributions.

Diseases of the Eye. A Hand-book of Ophthalmic Practice, for Students and Practitioners. By G. E. DE SCHWEINITZ, A. M., M. D., Professor of Ophthalmology in the Jefferson Medical College; Professor of Diseases of the Eye in the Philadelphia Polyclinic; Ophthalmic Surgeon to the Philadelphia Hospital; Ophthalmologist to the Orthopædic Hospital and Infirmary for Nervous Diseases. With 255 illustrations and two chromo-lithographic plates. Third edition; thoroughly revised. (*Philadelphia: W. B. Saunders*, 925 *Walnut St.*, 1899.)

The fact that the publishers have found it necessary in so short a time to issue another edition of the work of this gifted ophthalmologist is strong evidence that the fruits of his labors are speaking positively and that the "Hand-book" has won its success by supplying, probably more fully than any other American text-book on this subject, the wants of students and practitioners.

The author is to be congratulated upon such a substantial tribute to the value of what he has done for ophthalmology in this country.

The first edition of Dr. de Schweinitz's book was widely and favorably criticised, and it is unnecessary here to review at length a third edition. We note that paragraphs on the following subjects have been added to this edition: Favus of the Eyelids, Blepharo-chalasis, Koch-Weeks' Bacillus Conjunctivitis (Acute contagious Conjunctivitis), Pneumococcus Conjunctivitis, Diplo-bacillus Conjunctivitis (subacute Conjunctivitis), Parinaud's Conjunctivitis, Pneumococcus Infection of the Cornea, Mixed (Staphylococci, Streptococci) Infection of the Cornea, Schizomycetal Infection of the Cornea, Oyster Shucker's Keratitis, Fugacious Periodic Episcleritis, Röentgen Rays for detecting foreign bodies in the Vitreous, Retinitis Striata, Hereditary Optic-nerve Atrophy, Eucain and Holocain. While it is evident that the author is no advocate of the so-called mechanical theory of the origin of pannus (page 249), we think that he might have expressed his own views more positively with reference to this interesting process. The belief is gaining ground that pannus is the corneal manifestation of trachoma,—in other words, that it is an invasion of the cornea by the trachomatous process. The fact that the region of the upper lid is the seat of the intensest manifestations of trachoma is, we think, sufficient reason for the usual location of pannus, not because the granules are more marked in this region, but because the specific bacteria are probably there in greater numbers and purity than anywhere else in the conjunctiva, consequently the upper part of the cornea is peculiarly exposed to infection.

What the author says about the use of eserine in corneal ulcers (page 278) should be remembered, and we are in accord with him in thinking that atropine in such cases is the better drug,—indeed further than this, it has always seemed to us that eserine outside of its use in glaucoma, deserves a very insignificant place in ocular therapeutics, and that so far as its use in corneal ulcers is concerned, the condition of irritation is far more apt to be heightened than ameliorated.

The author quotes Nettleship (page 308) as saying that episcleritis is more common in men than in women. We have found just the reverse, and so also have Meyer and Stellwag. It would be interesting to know what the author's own experience has been in this connection.

It is not uncommon to hear students complaining of the great number of remedies and methods of treatment laid down in the text-books out of which a choice must be made. We think that the most effective and, in many respects, the safest teacher of ophthalmology to whom we have ever listened was one who was in the habit of delivering his opinions as axioms, who used very few drugs, and who rarely spent much time upon the rehearsal of other men's theories and suggestions. There is probably no science so rich in discarded theories and so hampered with worthless suggestions as medicine, and the text-book which banishes such material from its pages will be apt to leave the most lasting impression upon its readers.

The book which Dr. de Schweinitz has given us, we are gratified to see, bears throughout the mark of personal experience and is unusually free—except when essential—of "what others think." The chapters on diseases of the conjunctiva and iris (Chapters VI and IX) which are supremely important for students and practitioners are admirable, and did the limits of a review permit we might multiply examples of valuable observations and advice. We cannot close without calling attention to the accuracy and suggestiveness of the many illustrations (255), and to prophesy for this third edition of Dr. de Schweinitz's book no diminished measure of success.

R. L. R.

The Care of the Baby. A Manual for Mothers and Nurses. By J. P. CROZER GRIFFITH, M. D. (*W. B: Saunders, Philadelphia*, 1898.)

Although a manual for mothers and nurses, and not distinctly a work for the use of the practicing physician or one interested in the purely scientific side of the subject, the present volume contains so much excellent material, and is so admirably compiled, that it can be read with great advantage by any one who is interested in the care and proper bringing up of young children.

The book is written for the layman, or, rather for the lay woman, and for that reason the author has made use of a style and mode of writing which can be easily understood by her, and has avoided the many technical words and phrases which are so characteristic of the usual literature on this subject. This popular style, we think, will not only be of advantage to those for whom the book is especially designed, but has made the text such attractive reading that it is difficult to see how any one can take up the book without becoming interested in its contents.

The entire subject of the "Care of the Baby" has been most thoroughly taken up, and the author begins with a consideration of some points of importance to be observed by the mother and nurse during the latter part of pregnancy and labor. This is followed by chapters on the baby's growth, the baby's clothes, feeding the baby, exercise and training, the baby's nurses and rooms, and, finally, the sick baby.

There are so many excellent points throughout the entire volume that, in so short a review, it is almost impossible to give a just criticism. The section on feeding the baby is particularly good, and we are glad to see that the author has taken such a positive stand as to the duty of every mother to nurse her own child; and also that, in the consideration of the subject of artificial feeding, he has followed largely the rules laid down by Rotch, of Boston. Under the sections on exercise and training, and the baby's nurses and rooms the mother will find many valuable hints on the proper hygienic management, care, and moral training of her offspring, the importance of which cannot be possibly overestimated.

The chapter on the sick baby has been treated under the following headings: I. The features of disease. II. The management of sick children, and III. The disorders of childhood. The first of these divisions, that on the features of disease has, we think, the disadvantage of not being complete enough to be of value to the physician and probably too full and technical for the

mother, whose mind may be filled with so many apparent symptoms that she will be made very miserable by the slightest indisposition on the part of her child. It contrasts markedly with the section on the management of sick children, which deserves nothing but the highest commendation. Under the third section, on the disorders of childhood, a brief account is given of all diseases peculiar to that period of life, and especial stress laid on their nursing and management. The work is completed by a good appendix containing accurate directions and receipts for making various articles of diet and medicines and for giving baths, hot and cold packs, spongings, etc.

Dr. Griffith has avoided criticism by making the statement in his preface that "the chapter on the sick baby is not intended to supplant the physician, but is designed especially for mothers in emergency, where medical aid cannot be quickly obtained"; and in emphasizing the importance of this statement we feel that we are not doing wrong in recommending the book most highly to mothers, nurses, and physicians.

A Text-Book of Obstetrics. By Barton Cooke Hirst, M. D., Professor of Obstetrics in the University of Pennsylvania. (*Philadelphia: W. B. Saunders*, 925 *Walnut St.*, 1898.)

Professor Hirst is so very well known both as a practical obstetrician and a teacher of obstetrics that the title of this volume alone should be more than enough to assure its getting into the hands of the majority of specialists, general practitioners, and students of obstetrics throughout the country. The work is an admirable one in every sense of the word, concisely but comprehensively written, in a style which makes its reading more a matter of entertainment than the perusal of numerous dry facts and dogmatic statements, which is unfortunately so characteristic of many other books on this same subject. Frequent reference in the text has been made to the work of others, both in this country and abroad; but a laudable effort evidently has been made to avoid mentioning the long lists of names and the tedious recapitulation of literary productions, which, in the opinion of the author, only tend to confuse and to complicate matters for the student. Hence, only the epoch-making articles have been referred to.

The illustrations of the book are, for the most part, excellent, and although some of them cannot be said to come strictly into the category of art, yet they have the advantage of bringing out the points which the author wants them to show. Exceptions to this might be made, however, in the case of a few reproduced photomicrographs, which occur in the section on the placenta. Photomicrographs may be scientifically accurate from the purely optical standpoint, but it is so very rare that one sees the reproduction of one of these pictures showing what is claimed for it, that it is with considerable regret that we see them, however few, in a publication possessing so many other advantages.

The author has divided his subject into the following sections: Pregnancy, Physiology and Management of Labor, and the Puerperium, the Mechanism of Labor, the Pathology of Labor, Pathology of the Puerperium, Obstetric Operations and the Newborn Child.

The section on pregnancy is, in the main, excellent, and offers no points for criticism, except that possibly enough stress has not been put upon the development of the fœtal appendages; we do not mean by this that there should be anything like a full treatise on human embryology in this place; but the development of the placenta with its relation to the decidua and uterine wall is so important a subject that we think a little more space might have been allotted to it. The diseases of the fœtal appendages, placenta, membranes, decidua, etc., are considered immediately after the question of their development. This is a new departure, for these subjects are, in the majority of text-books, given a section to themselves, and put later in the volume. Their consideration, however, at this time and place may have distinct advantages, for, clinically, many of these conditions cannot be recognized until after labor, and when put under a separate heading, as is usually done, the student may get the idea that they are desperate diseases to be treated *per se*.

Too much credit cannot be given to the masterly manner in which the author has presented the subjects of the management of normal labor and the puerperal state, but it is difficult to see why these subjects should have been taken up before the mechanism of labor has been considered.

The treatise on pelvic contraction and deformity, and labor when complicated by such conditions, is an excellent one in every possible sense of the word. This section appeared a few years ago in the first edition of the American Text-Book of Obstetrics, and to those who are familiar with this work it needs no recommendation.

We are somewhat surprised that the author has not mentioned the importance of a bacteriological diagnosis, by means of the uterine culture, in puerperal infection, nor can we agree with him in thinking that in many cases the repeated, frequent douching of an infected uterus to be of value, for in our experience such cases are by no means the rule. He also advises the routine use of the curette; and strong (1-2000) bichloride intra-uterine douches; upon this point we must also confess that we are skeptical. In our opinion the treatment of puerperal infection and the determination as to whether we shall use the curette and douche are directly dependent upon the nature of the infection as indicated by the bacteriological findings in the uterine lochia. Except the above, the section on puerperal infection is good.

Operative obstetrics and the section on the care of the new-born child are both well worked up, though that on the new-born child is short and more might have been said on the subject of infant feeding.

BOOKS RECEIVED.

Nervous and Mental Diseases. By A. Church, M. D., and F. Peterson, M. D. 1899. 8°. 843 pages. W. B. Saunders, Philadelphia.

On Fractures and Dislocations. By Professor Dr. H. Helferich. Translated from the third edition (1897) by J. Hutchinson, Jun., F. R. C. S. 1898. 8°. 162 pages. The New Sydenham Society, London.

The Pathology and Treatment of Sexual Impotence. By Victor G. Vecki, M. D. From the author's second German edition, revised and rewritten. 1899. 8°. 291 pages. W. B. Saunders, Philadelphia.

Transactions of the American Pediatric Society. Tenth session, held in Cincinnati, June 1, 2 and 3, 1898. With an index of Vols. I to X. Edited by F. M. Crandall, M. D. Volume X. 1898. 8°. 226 + xii pages. Reprinted from The Archives of Pediatrics.

American Pocket Medical Dictionary. Edited by W. A. N. Dorland, A. M., M. D. 1898. 16°. 518 pages. W. B. Saunders, Philadelphia.

Proceedings of the American Medico-Psychological Association at the Fifty-fourth Annual Meeting, held in St. Louis, May 10-13, 1898. 8vo. 417 pages. Published by American Medico-Psychological Association.

Annual Addresses of the President of the Medical Society of the District of Columbia. Delivered 1894-95-96-97-98. By Samuel C. Busey, M. D., LL. D. 1899. 8vo. 178 pages. Washington, D. C.

The British Guiana Medical Annual. Tenth year of issue. Edited by W. S. Barnes, M. D., and J. F. S. Fowler, M. B. 1898. 8vo. 52 + xxxiii pages. Baldwin & Co., Georgetown, Demerara.

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THE DUTIES AND THE DANGERS OF ORGANIZATION IN THE NURSING PROFESSION.*

By George M. Gould, M. D., *of Philadelphia.*

When I received the kind and honoring invitation of your committee to speak to you to-day I chanced to be chatting with a friend; I read the letter to him and asked him what I should do. His answer was a description of his personal efforts in behalf of nurses and their calling, efforts extending over many years, and most unselfishly carried on. The general effect was not encouraging to me. My friend could not see how he had done any good to others while he had sadly wasted his own time and life, to find at last that he had aroused only suspicion and had ended in resultlessness. When I came to ponder the matter I thought I had found the solution of my friend's pessimism in the fact of the needs, difficulties, and dangers of organization, and that in the swift historic uprising of your large body, these needs, difficulties and dangers must at first necessarily end in much confusion and disappointment. All human institutions reach a condition of stable equilibrium through manifold trials, and the trials should not deter us from adding our personal influence as one factor that may, or, it is true, that may not have influence in determining or hastening progress. If our contribution is ineffective, we must remember that in science a negative experiment is always of value. We must learn the "No thoroughfares" of life for the first time and before signs have been put up across them, by actually running against them and thus experimentally proving that there can be no advance in that direction. Moreover, some later Baron Haussmann of progress may be able to crash the Boulevard of Science straight through the obstruction that we, in our impotence, deemed insuperable.

I shall say but a passing word as to the need of organization,—and that consists only in the emphasis of its inevitableness. You find yourselves in a somewhat chaotic condition to-day so far as pertains either to social, national, international, or professional organizations. But in these times of a thousand kinds of "combines" and concentralizations, there is no escaping the evolutional fatality of union. I use the word "fatality" advisedly because I would at least hint by it my feeling that there are cruelties and dangers of many kinds almost inevitably connected with any very thorough organization,—not enough to make us refuse to join, but surely enough to make us cautious. Majorities are tyrants and democracies are as tyrannous as any other type of government. The very forces of cohesion which compel like units to bind themselves to solidarity and unity of purpose have an

*An address to the Graduating Class of the Johns Hopkins Hospital School for Nurses, delivered June 2, 1899.

inherently fatal tendency to crush out the independence of the units and to reduce effort to a huge and ungovernable mechanicalism in which freedom is sacrificed to the attainment of object, and method is scorned for result. Up to now you illustrate none of this, and my warnings may seem very much like foolish croaking. I learn, indeed that your class is an instance of the good of organization, and with all my heart I congratulate you on the fact that the educational ideal has been uppermost in your three years of work, and that you have not been bribed and whipped to do an atrocious amount of slavish work for the benefit of some heartless institution, which pays you in a sheepskin, the significance of which lies in the knowledge fought for despite jaded bodies and minds. But the point of my croaking is that you compare the lots of many of your sisters in other training schools which demand so many hours a day of toil that the educational aspect is lost sight of, and is impossible for the weary ones. *There* you see the evil of organization.

In a calling like yours and, I may add, like mine—that of the nurse and the physician—the need of organization is most evident, and yet there is a strange waywardness, an unaccountable shyness which preserves freedom and individualism by an aloofness that serves at least as an excellent "governor" of the machine, and which keeps it from self-sacrifice to ultra-mechanicalism. For many years, in season and out of season, I have been pleading for a unitized medical profession and the dire consequences of our disorganization have never been more frightful than to-day. But none would be more prompt than I to delimit sharply the range of action of medical organizations, should they seek to tyrannize over the righteous freedom of the individual member.

In your calling and condition the duties and dangers of organization are greater than in almost any other. Among several reasons for this there is one that I trust you will pardon me for alluding to. I may do this the more freely because I have a hundred times urged the greatest liberality toward and encouragement of the desires of women for a wise equality of opportunity with men. But no such generosity need blind us to the fact that by nature woman in her uses of social power and organization is a "born tyrant." In the purely personal relation she is grace divine, but whenever put in authority over others, and especially over other women, she usually manages to make herself as hateful and as well hated as human ingenuity will permit. It is, of course, not always so, and thank God for the blessed exceptions! In organizations of women, women must necessarily be officers, and of course majorities must rule. It strikes me therefore in selecting the officials of whatever organizations you may form, you should use your best endeavors effectually to squelch politicians and tyrants and to reward those who show *das Ewig-Weibliche*, the graciousness of justice, and the justice of graciousness, in the exercise of authority and power. In governing, for Heaven's sake do not learn of us men only our faults while you assiduously forget both our virtue of justice and yours of love. The hardest duty you will have to learn is that of kindness and justice to minorities. Politically, the most tyrannous of human beings and the most enslaved is the American. Can you not manage it so in your treatment of those who do not vote with the majority, that you do not march over their rights with the ruthlessness which is fast reducing the terms Democracy and Republicanism to hideous jeer-words of inverted significance?

The roots of institutions and of organizations too frequently spring from the richly manured depths of selfishness. The commercial doctor is despicable enough; do not add the commercial nurse to the terrible burdens under which humanity must stagger!

If the spirit of trades-unionism gets control of your societies and organizations, I hope they will quickly be blown to utter smithereens. The very essence of your life, the heart of your work lies in the personal relation, the wooing back to health and life of bodies and minds hurt in the world's financial warfare. Send metal, even gold, instead of blood, into your hearts, and you may have very perfect corrosion-images of the cardiac structure for the laboratories of the future nurso-pathologist, but you will then be deservedly dead while the pathologist will be lecturing learnedly upon your fatal disease. I beg that you will keep the financial relations to your patients utterly out of the reach of your laws and by-laws and resolutions. This is absolutely a personal matter to be governed by your character, your ability, your whim and fancy, and by your patients' condition in life; I hope you will withdraw from any society that in the least attempts to govern you in this matter. Money you must have to live by, as must all of us. Nursing is your trade; it must give you the means necessary for carrying on your trade; but if you wash dishes for money alone they will be dirty dishes when they leave your hands. When your work is an art and when it is with the material called life, the rule holds all the more strenuously; the great God of Life will not allow you to have a master above Him!

This brings us logically to a thought concerning the relation of the nurse to the family of her patient. There is one pretty effective answer to the impertinence of some families which would look upon the nurse solely from the employer's point of view. If you let such upstarts see that the financial motive is the dominant one in your mind and in your organizations, your answer to the one impertinence is only by another: *I'm as good as you!* But the killing reply to all false pride is the acted one: *I am in truth better than you,*—that is, I will prove to you that I am more unselfish than you. To those who would positively or negatively treat you as a kind of servant paid for by your demanded wage, you may, as does the true physician, teach a nobler way, both by word and action, that while the laborer is indeed worthy of his hire, the hire is not by any means the worth of the laborer.

Not the least of the dangers to which as an organization your guild will be subject is another kind of subserviency—to the physician and to his profession. To steer clear of the Scylla of a too smart independence and the Charybdis of a too decided servantship will task the tact of the best of you. In all matters pertaining to therapeutics, of course you must be unflinchingly loyal and even obedient to the medical man's orders. And yet you have your own individuality, and, as an organization, yours should be an entity subject to your own corporate ideals and conditions. There has been much criticism of a tendency, for the existence of which I cannot

vouch, for the nurse to supplant the physician. Many nurses are doubtless wiser than many physicians, but tragedy awaits that nurse who is conscious of the fact, at least if she even whisper it to the person in her mirror!

I suspect the nurse's greater danger lies in the loves and hates of partisanship. "Her favorite doctor" is liked altogether too much, and the one she does not fancy is not half so bad as she thinks. It may be that she needs to rid herself of all such likes and dislikes and fix her attention upon the impersonal aims and needs of her calling. I have heard of chief nurses who turned hospitals topsy-turvy and transformed training schools into hotbouses of evil and cliqueism by assigning hated nurses to detested physicians, or by working her girls to death, and other such petty savageries. It is sad,—but possibly the world will be better when you all become head nurses and superintendents!

The business conduct of your organizations will need careful looking after. To be effective, charity itself must become a business. Some wise unwise mot-maker has said that charity is the basest of human passions. Doctors are proverbially bad business men, (though I do not believe they are quite so pitiable as they are represented) but surely despite all their native shrewdness in buying and selling, women will probably commit grievous business errors in conducting their organizations. A lawyer-like prudence is demanded nowadays to guide any great movement right. The friend of whom I spoke tells me that a most excellent scheme of an insurance or beneficial organization for the benefit of nurses went all to smash after great efforts and partial successes because of—but that is another story! Would it be rank heresy to suggest a cool, legal, male brain as an adviser even to the wisest and best of women? Surely the Red Cross Society has lately demonstrated with appallingly glaring colors the need of such a head. When an organization handles millions of dollars without accounting for a cent, it is high time that sane men and women should pinch themselves to see if they are really awake or not. You need to make every training school in America demand a free three-years' educational course with only 8 hours a day devoted to practical work; you need a great journal devoted to your interests and your progress; you need something corresponding to an insurance company adapted to your peculiar conditions; you need a post-graduate school for superintendents; you need a systematization of your business, how to find work, how to supply country towns and farms with trained nurses, where to secure special training, and how to find the people wanting that kind of specially trained nurse, etc.; you need nurses' houses or homes, where you can meet each other, and have something like a home when you are off duty; you need special loan-libraries; you need laws to protect your calling from the scandal of the corrupt, who, for purposes of gain and immorality, don the garb of the nurse; you need a rigid ordering of your relations with the city, the State, and the National Government, and particularly with the military departments; you need an energetic national and even an international organization, and for all these and other things you need wise and clear business heads to govern and to guide you, and to mold your guild into one of the great agencies for alleviating sociologic ill and for bringing about a more lovely civilization than we have so far dreamed of.

And, with it all, will you hate quackery more than you do the devil himself? Already the quacks, those pathogenic microbes of the profession of medicine, those verminous parasites of poverty and ignorance, are quoting Trained Nurse So-and-so as endorsing such and such a concoction or contraption for the magical cure of all disease. I beseech you by all that is holy and of good report, that you renounce this wickedness! When the official head of a representative American nursing organization officially sprawls over and through the advertising pages of the yellow newspaper as a limitless endorser of "Greene's Nervura" and of "Electropoise," it behooveth you to haul up sharp and see that your skirts do not draggle even in the shallowest of these filthy puddles!

I wish I could say something of use, and that might encourage you to add your influence in providing an effective and systematized service of trained nurses for the United States Army. Whether in peace or in war (except perhaps in the front during actual battle) the army needs you. The lack of such an organization with its resultant terrible morbidity and mortality among the sick soldiers during the late Cuban skirmish was demonstrated beyond all doubt. The Nurses Associated Alumnae of the United States and Canada at their second annual meeting in New York about a month ago, took up this important matter, and are earnestly trying to secure the passage of a bill by Congress to bring about the desired object. In this way only can the business be systematized, the wasted efforts of competing organizations neutralized, and as Carlyle would say, the work get itself done.* Another good that would follow the establishing of such systematization would be the disappearing forever and ever, world without end, amen, of the advertising self-seekers, the quack doctors posing as philanthropists, and the silly mob of the charity-becrazed sentimentalists, all buzzing about with their incapacities and fatnities like the myriads of Blue-Bottle Flies of The Four Little Children, described in a wise geographic book actually written before the Hispano-American War.†

Women may be divided into three classes, the Good-for-somethings, the Good-for-nothings, and the Unspeakables. There is nothing which fashion hates more than the first class. In its heart it likes the third class far more. With

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*In our imperialism-craze you must suffer for the sins of your rulers, and must prepare yourselves to meet the demand for nurses in tropical countries where in the name of liberty we are shooting down those who ask for liberty. The English *Colonial Nursing Association* was formed in 1896 to provide specially trained nurses for England's colonies in all parts of the world. The *Lancet* makes the wise suggestion to try to train up a school of native nurses. Here is a great work for you also.

†"And on the signal being given all the Blue-Bottle Flies began buzzing at once in a sumptuous and sonorous manner, the melodious and mucilaginous sounds echoing all over the waters and resounding across the tumultuous tops of the transitory titmice, upon the intervening and verdant mountains with a serene and sickly suavity only known to the truly virtuous."

the sharp X-ray eyes of moralized intelligence, look through the walls and roofs of a vast number of modern homes and you will find doless daughters whom their parents are trying to get rid of, and doless wives who, money alone excepted, are trying to get rid of their husbands.

When servant-girls marry, the first thing they demand is a servant-girl. Shop-girls—I beg pardon, I mean Salesladies—must not work after marriage, they must ape the vices of the second class of ladies who scorn their too perfect flatterers. Lazy, cunning, pretty, empty-headed, and empty-hearted, the young ladies of the foolish ill-to-do well-to-do, while nursing their hysterics, and their flaccid muscles, manage to twist ever tighter the silken bands whereby, sitting at the center of the commercial economic slaveries of civilization, they draw into their laps the stolen products of human industry and cruelty, avid to get the most and give the least. But even here are awakening, thank Heaven, an increasing number of women who, like Doré's monk, are looking about them with horror and alarm, and are determining that *their* lives at least shall not sink into the degradation of spiderhood. Yours is the splendid proving that there are at least ten thousand American women unsatisfied with araneal ethics.

In other reactions from spiderliness we have many sad morbidities, the "New Woman" being not the very least. Perhaps the "New Nurse" is to be another if she is not wise and wary. Institutional medical charity justifies all the bitterness wrapped in the jibe that "charity is the basest of human passions." If it is incapable of turning all the milk of human kindness to bonnyclabber and even to mitey cheese, if it cannot at one stroke and directly pauperize the patient, curse the giver, and debauch the medical profession, it labors hard to do it by indirection; then if all plans fail, trust some advertising medical college for getting hold of several hundred nurses and making them help the Professors to attain notoriety, students, consultations and iniquitous state appropriations! Organization and Institutionalization may be good things for you, but not unless you are somewhat wiser than serpents and more shy of nets than are many doves.

The most powerful antidote for the evils of malorganization or over-organization, and for the dangers that beset your future career, I believe will be found in the very nature of your calling and in the goodness of the human heart, which rarely fails to respond sympathetically to the cry for help by the suffering.

And this work of yours is so good, and will only remain so good, if you refuse to allow any institution, or rules, or organizations to come between you and your patient. Your calling is of the best and most truly evolutional (not revolutional) because it continues the kind of occupation and by the same methods you have inherited from Mother Eve,—personal work by personal methods. The giving of love, care, helpfulness, sympathy, nurturing, nursing,—what else has woman done in the world? What better thing could any being do? The female man-imitators are doomed! Is evolution a word, a philosophy, a thinker's game of thought, or is it the most actual of facts and the most inescapable of biologic laws? There can be no rejection of the law of heredity. The habits of a million ancestors are commands which we seek to break only at our infinite peril. The fact, of course, is that each of our personalities is the last link of the biologic chain which binds us to the infinite number of our ancestral organisms, and God, if you please, has yet some control of the cosmic process! He will hardly permit the last link to cut itself from the past and set up as an independent existence. The ghosts of all history unite in and direct each individuality. Strength and effectiveness consist in obedience to their orders.

There is one way in which organization can help you, if you, as you must, use it as a tool and not allow it to use you as one. This consists in making it a means whereby you come to your patient. The hospitals have half turned you into servants,—they at least are well supplied with nurses, so we may leave them out of the count. Then the rich have you at command; for we are all the slaves of the plutocrats. Upon them then we may waste no thought or sympathy. The poor, *i. e.* the very poor of the cities, can also command you, through the hospitals. But there are far more needy, more numerous, more worthy classes to whom neither you nor your societies, I fear, have hardly given a thought. Among these are the farmers and the people of small villages. These constitute the great majority of the good people of the United States, and they do indeed need your advice, skill, knowledge, and help, quite as much as do any city-folk. Ignorance and disease await you there fully as much as they do in crowded places. It seems to me that one of your primal duties of organization is to secure a machinery of distribution whereby you and your knowledge of hygiene, the knowledge *par excellence* of the trained nurse, shall be brought to the country and to the village. Genuine missionaries you must be to carry the gospel of nursing to your far-away over-worked and untrained sisters of a million country and village homes, and to the sick ones there.

The reckless poor and the reckless rich of the cities, as we have seen, are well nursed and provided for; they are your masters. But let it no longer be said that "none but a pauper or a millionaire can enjoy the luxury of a nurse." You have yet to organize a machinery to reach the wants of the great and more deserving middle classes. To this class let us add another that still more acutely touches our sympathies,—the proud and self-respecting poor of the cities, who, no worse off financially than the spongers, have as yet not been bribed, corrupted, and herded in the hospitals and almshouses by the professional philanthropists and the selfish charity-mongers. It seems to me that your most pressing duty is to these two sets of people. The clerk, the prudent workman, the little shopkeeper, the working woman, etc., with incomes of from three hundred to one thousand dollars a year—these cannot afford to pay you twenty dollars a week for your services. And if this is so, those with still smaller incomes can afford to pay you but a small percentage of this amount. And for that matter, is your conscientious, skilled, and devoted help for seven days and nights, not really worth far more than twenty dollars? Remember too that your profession is fast filling and like every other, filling to overflowing. Give, then, in advance and in chosen cases, before pitiless competition forces the wage-limit down. But that is a deplorable argument; so let us return to the more gracious, eternally-to-

be-repeated, eternally forgotten, *Noblesse oblige!* Wage-pride in a nurse or a physician is the devil in the pulpit; it is Croker and Quay throned and lording it as statesmen. In this matter I beg and beseech you to think of the duty and the blessing of grace, and the gift of yourselves. Most other giving than self is, in the last analysis, but a fraud and a delusion. Whether you will or will not, you are, if not copartner of the medical profession, at least a chief assistant; and the tradition and the practice of the members of that profession is to give on the average at least one-third of their lives to the needy and suffering, without thought of compensation in money. Verily, verily, I say unto you that you must go and do likewise! If you wish us to love and honor you, that is the surest way to command our honor and love. By what means? Quickly comes the answer: First, by individually meeting the need of the needy with your service, or a part of it, at a price or at no price, corresponding to the ability to pay; Secondly, by means of the Visiting, or District, or Instructive Nursing Society. If there is no such society where you live, then establish such a society! Start it with a membership of one; get others to join; plan it out, work it out, with the help you can and will find if you do really wish to find it. If the established society works badly, if it is the outcome of dilettantism and unbusiness-like sentimentalism, set to work to put it in better order. All things are possible to the resolved woman!

The Instructive District Nursing Associations of Chicago and of Boston, seem to be models. These and similar societies have recognized the profound need of teaching the members of the families among which they go how to become good nurses; how by example and precept to care for each other and for themselves, and in a hundred ways to brighten and purify their lives. A nurse is not a good nurse unless she is a good teacher and inspirer of others to emulate her skill, neatness, and unselfishness. In district nursing one has a greater variety of cases, more out-of-door exercise, greater freedom Saturdays and Sundays, etc. One also, I think, does more good and leaves more lasting impressions. There is a commingling of pathos and fun that is altogether blessed, and seeing more life, one's own character is broadened and sweetened. In the choice and method of carrying on an occupation, the purer the purpose and the more earnest the emotion, the closer must one come to actual life. All desire to get away from the blood and muscle and heart-throbbing of actuality, ends in resultlessness, ennui, and even in downright sin. Keep your finger on the pulse of life if you would know how the heart of life is beating. But all who can, must be made to pay for the work and for the teaching. Selfish charity is very pleasant but it is very iniquitous. Nay, more, all charity is a curse unless it seeks to do away with the need of charity. You must not let your noble calling degrade into vicious relief-doling.

Is aristocratic flummery and class-prejudice beginning to appear among you? I hear whispers of the fact, and in some of the literature I have glanced over, especially in that emanating from England, it crops out in amusing innocence. I have found there such recurring expressions as "Nurses of high birth," "of lower birth," etc. I am treading on dangerous ground perhaps, but I trust that there is sufficient Americanism in you to scorn such long-eared nonsense. Neither in your speech nor in your hearts let such expressions and distinctions arise. If in the sisterhood of nations our country has any function it is surely to show the unchristianity, the untruth, and the unscience of such prides and such lack-o-prides. The only professional or scientific significance of such terms I can imagine is the obstetric one:—the high-birthers must have entered the world after the manner of Caesar! The common fashion of the low-birthers seems preferable! But I hear that the high-birthers make the best nurses, are better for the instructive and district nursing societies to employ, that they are better received in poor families, that they are not so "stuck up" as regards what is called menial work, etc. Let every low-birther make it her chiefest point of pride to disprove this!

Let me read a few sentences from the history of the Mayflower people by one of them. They surely were low-birthers if there ever were any such:

"But that which was most sadd & lamentable was, that in 2. or 3. moneths time halfe of their company dyed, espetialy in Jan: & February, being ye depth of winter, and wanting houses & other comforts; being infected with ye scurvie & other diseases, which this long vioage & their inacomodate condition had brought upon them; so as ther dyed some times 2. or 3. of a day, in ye foresaid time; that of 100. & odd persons, scarce 50. remained. And of these in ye time of most distres, ther was but 6. or 7. sound persons, who, to their great comendations be it spoken, spared no pains, night nor day, but with abundance of toyle and hazard of their owne health, fetched them woode, made them fires, drest them meat, made their beads, washed their lothsome cloaths, cloathed & uncloathed them; in a word, did all ye homly & necessarie offices for them wch dainty & quesie stomacks cannot endure to hear named; and all this willingly & cherfully, without any grudging in ye least, shewing herein their true love unto their friends & bretheren. A rare example & worthy to be remembered. Tow of these 7. were Mr William Brewster, ther reverend Elder, & Myles Standish, ther Captein & military comander, unto whom my selfe, & many others, were much beholden in our low & sicke condition. And yet the Lord so upheld these persons, as in this generall calamity they were not at all infected either with sicknes, or lamnes. And what I have said of these, I may say of may others who dyed in this generall vissitation, & others yet living, that whilst they had health, yea, or any strength continuing, they were not wanting to any that had need of them. And I doute not but their recompence is with ye Lord."—*The Bradford History of the Plymouth Plantation.*

"Servants of the poor" is another term used by orators to graduating nurses and by writers of mock heroics. It is quite highfalutin—and quite silly! I trust you will not go to your life-work a victim of any phrase-maker's tricks. Your first duty, like that of all of us, is to see facts; your second, is to know facts; your third, is to make facts. If you must dub yourself with any other titles and think of yourself as anything less or more than a nurse—quite a noble and ennobling name, I think—is not the word *friend* enough? A servant you must not be, a patronized or a patronizer you dare not be. Friendship is what is needed by the patient and by his family. The friend may teach and help, not serve or patronize; he must always sympathize with and love.

You may gather that I have a more vivid feeling of the

dangers than I have of the benefits of organization, and I shall not very emphatically deny the charge. The shame and infamy of anti-Dreyfus France, the degradation of American boss-politics, the cruelty and selfishness of monopolies, our pension demagogery, such things are ever before our eyes to warn us against giving up our freedom and our honor to any organization. The hardest of all problems you will have to solve will be to secure the good things that are obtainable only through organization and at the same time to avoid the evils so generally the consequences of organization.

It is only by means of money that one can get that which is worth more than money, and that which money cannot buy. Just so it is only by means of organization that you can obtain that which organization alone cannot give. This means, of course, that you must use the power derived from organization as a mere instrument. There is nothing more harmless, neutral and unorganized than water—the oceans of it that cover so much of the earth. There is nothing more symmetric and beautiful than a snow crystal; but transmute an ocean into a polar ice-cap, and death is its command, even to the wandering splinter of it called an iceberg. Let love and ethics fail for a day to use, fill and thrill your organizations, and the devil will surely seize upon them and make them serve his purposes.

In the polar regions of our earth the cold is so intense and continuous that ice and snow are always forming and it is impossible to say what would be the disastrous consequences as regards the temperature, climate and vegetation, even the life of the entire globe, were it not for the existence of one great countervailing fact: Up from the great oceans of the equatorial and temperate regions softly creep the massive currents of warmer water, until approaching the poles, they dip deeply downward beneath the arctic ice-cap, and spreading through these freezing ocean abysses, they bring the melting messages from the far-away sun, from summer days and smiling climes. Your work in life seems wonderfully like all this. However lethal and frightful our civilization, it shines with such splendid and alluring auroras that into it with reckless fatalism press the infatuated discoverers and travelers from lands where labor wearies and deadens, and where love is becoming the legend of idle singers of empty days. Over this white waste of frigid expanse deepen the glaciers of selfishness, and glitter the ice and snow of luxury and of greed. Among the influences that prevent this palsying congelation of death from crawling and crunching through the whole wide world, comes Love! And what love is purer and more vivifying than that of you workers, what more heartening than that which gives itself to win back to health, to hope, and to life, those who have been broken by disease and worn by suffering? Yours the privilege, cosmic and yet personal, of throbbing beneath and through the bitter chill of an icing civilization the softening warmth of divine beneficence and love!

A PIN IN THE VERMIFORM APPENDIX.

By James F. Mitchell, M. D., *Assistant Resident Surgeon, The Johns Hopkins Hospital.*

In the Johns Hopkins Hospital Bulletin, Nos. 94, 95, 96, January, February, March, 1899, was published a collection of thirty-five cases in which pins had been found present in the vermiform appendix, or had been the cause of attacks of appendicitis.

Since this publication a most striking case has appeared in the service of Dr. Halsted, and in connection with the subject seems worthy of record.

History.—W. O. R. (Surg. No. 8898), a colored boy, aged seven years, was admitted to the surgical wards April 26, 1899, complaining of "cramps in the stomach."

Since he was two years of age he has suffered from repeated attacks, with abdominal symptoms referable to the right iliac region and accompanied by pain, tenderness and vomiting. These have recurred at intervals of a few months for the past five years, the duration of the attacks varying from a few days to one or two weeks. The intervals have never been completely free from local symptoms.

No history of the ingestion of a foreign body could be obtained from the parents.

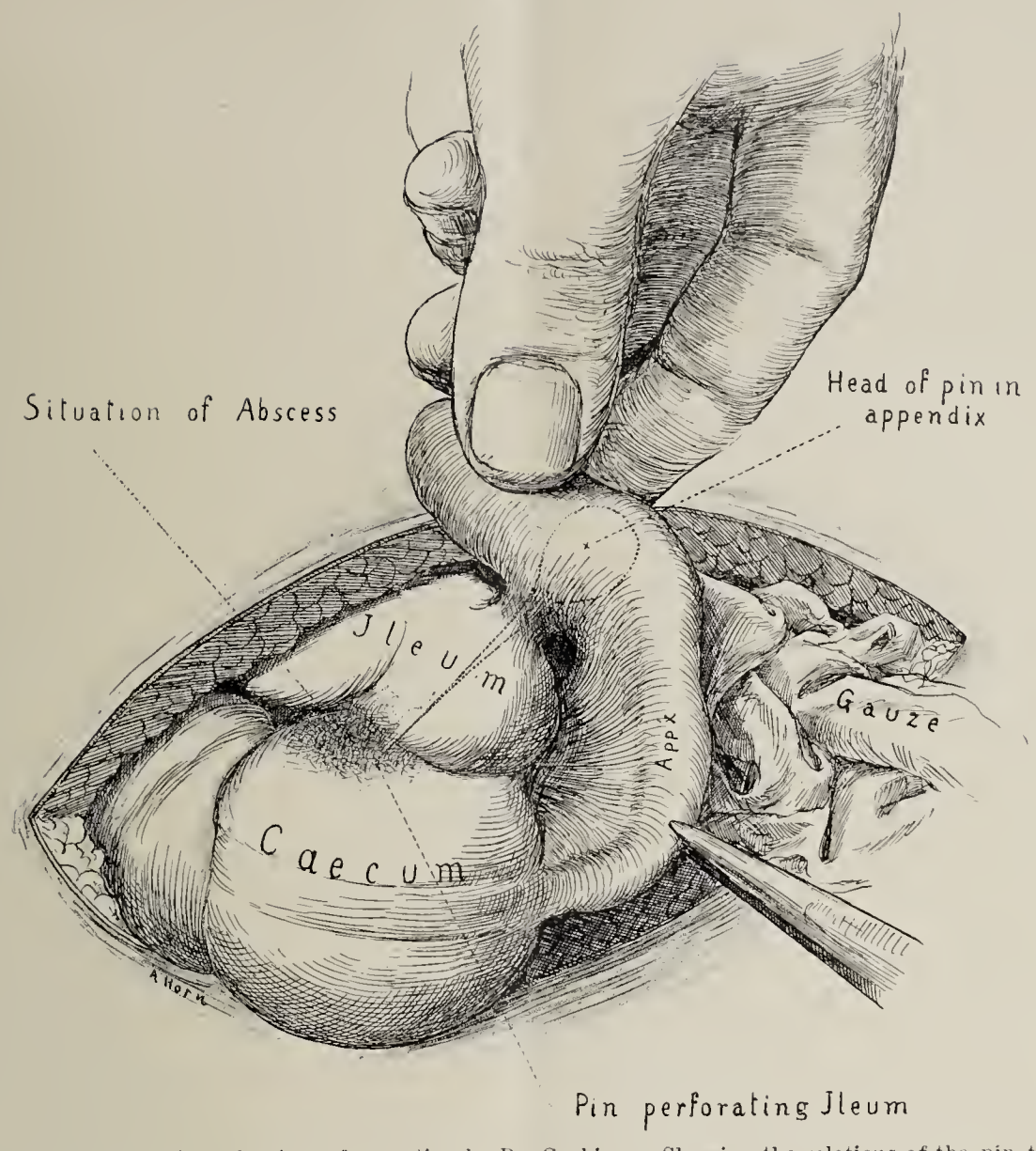
On April 22 (four days before admission) he complained of feeling badly, and of a feeling of tightness in the abdomen followed in a short time as usual by cramps and vomiting; no chill; not much apparent fever. Since onset there have been paroxysms of pain about the navel, the attacks lasting three or four minutes and being so severe as to cause him "to be doubled up." Abdominal tenderness has been marked; bowels constipated, one movement yesterday, after medicine; no pain on micturition, but increased frequency.

Examination on admission (Dr. Cushing). "Well developed colored child with slightly pinched facies; lying on back with knees drawn up. Pulse compressible, rather poor quality. Tongue has a diffuse, thin, white coating. Respiration costal in type; abdominal movements slight. *Abdomen* slightly and symmetrically distended. Child protects right iliac region with hands. Dulness over whole of right iliac region. No dulness in left flank. Abdominal spasm and rigidity limited to right iliac fossa render palpation difficult. There seems, however, to be a mass in the right iliac fossa. Temperature 103.2°. Leucocytes 11,000." He was prepared for immediate operation.

Operation under chloroform anaesthesia (Dr. Cushing).

Laparotomy for appendicular abscess. Evacuation of abscess. Appendectomy. Pathological anastomosis of tip of appendix with ileum, through which a pin passed, producing a perforation in opposite wall of ileum. Closure of two appendicular communications. Drainage.

Under anaesthesia the tumor was found to occupy the



From a sketch at the time of operation by Dr. Cushing. Showing the relations of the pin to the appendix, ileum and cæcum.



The appendix and pin after removal. Showing the pin encrusted with fæcal matter.

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whole right iliac region from median line to level of umbilicus. Incision was made over the tumor through outer border of rectus muscle, and subsequently enlarged, dividing the epigastric vessels. The abdominal wall was oedematous. The tumor mass was covered by a layer of infiltrated omentum, which was adherent to anterior parietes. Adhesions were freed and walling-off gauze placed about the mass at points of approach to the free cavity.

The tumor mass was attacked and an abscess containing about 15 cc. of bad smelling flocculent pus evacuated. Coverslips showed some bacilli, no streptococci.

The *appendix* was sought for and finally freed from the side of the tumor mass. No perforation could be made out in the appendix. The abscess was situated at some distance from it lying between cæcum and ileum. The appendicular serosa was not markedly injected. The appendix was found to have a double communication with the bowel; one at its base and another about 2 cm. from its tip, where it anastomosed with the ileum by a free communication opposite to the mesentery.

In the appendix opposite to this communication a hard, round body, the size of a hat-pin head, could be felt, and running from this through the passage into the ileum extended the shaft of a pin, the point of which reached the abscess some distance away.

The meso-appendix was tied off and the appendix amputated at its base, the stump being inverted into the cæcum. The communication with the ileum near the tip was treated in the same way, the opening into the ileum, which was lined by mucous membrane, being closed by three mattress, Halsted sutures which had been placed before the division.

The seat of operation was drained with iodoform gauze and the abdominal wound partly closed.

The patient took the anaesthetic well and had no bad symptoms referable to it.

The operation was performed in the afternoon and the child seemed in good condition at its close, although the pulse was rapid—134. During the evening he was comfortable and apparently doing well. Frequent salt-solution enemata were given to relieve thirst. At midnight he was seen by Dr. Baer, the ward surgeon. The pulse was then 116 and of fair volume and the patient complained only of slight pain.

At six o'clock next morning the nurse noted no change in his condition; pulse slower. Happening to pass his bed a few minutes later she noticed his eyes rolled up and glassy, and was unable to rouse him. Attempts to resuscitate him were unavailing and he died at 6.45 a. m.

Autopsy (Dr. MacCallum) showed localized peritonitis, about cæcum; broncho-pneumonia of slight extent; great enlargement of thymus; small hemorrhages about thymus and mediastinal tissues; moderate glandular hyperplasia.

No definite assignable cause of death.

Bacteriology.—Bacillus coli communis and an unidentified bacillus were obtained from the appendix. (Dr. Clopton) cultures from the heart, spleen and thymus gland were sterile. Pneumococcus was gotten from the lungs, and from the kidney and liver bacillus coli communis. Cultures from the kidney, liver and peritoneal cavity gave an unidentified bacillus, probably proteus Zenkeri.

THE PRESENCE OF TYPHOID BACILLI IN THE URINES OF TYPHOID FEVER PATIENTS.

By Norman B. Gwyn, M. B., *Assistant Resident Physician Johns Hopkins Hospital.*

It has been frequently shown that typhoid bacilli may be present in the urine of typhoid fever patients and convalescents and that the danger of infection from this source was seriously to be considered; up to the present time, however, we have completely overlooked this question, and systematic disinfection of the urine has never been perfectly, if at all, carried out. If the presence of these bacteria in the urine were but an occasional happening and associated always, as in some cases, with urinary disturbances marked enough to attract attention and arouse suspicion, no great danger of infection need be feared, but their occurrence in 20 to 30 per cent. of all cases, often in urines presenting slight if any alteration, makes it very evident that in the spread of typhoid fever the urine plays a far greater part than has heretofore been suspected. Bouchard, in 1881, seems to have been the first to describe this condition, his investigations showing bacilli in 50 per cent. of cases; faulty differentiation of the typhoid from colon bacilli may have given this high percentage.

Hueppe, Seitz, Konjajeff, Karlinski, Neumann, Borges, de la Faille give varying results in describing the same condition. Hueppe finding bacilli but once in eighteen cases, Karlinski in twenty-one of forty-four. Blumer, in this hospital, investigating pyuria in typhoid fever found typhoid bacilli twice in sixty cases. Wright, of Netley, obtained typhoid bacilli in the urines of six of seven cases. Besson in six of thirty-two. Neumann noted that the bacilli were usually in pure culture and were often so abundant as to render fresh urine turbid, the urine remaining, however, acid in reaction; the evident danger of infection is emphasized by this writer and others.

More recent work has been done by Petruschky, Horton-Smith, and Richardson. Petruschky, though obtaining bacilli but three times in fifty cases, dwells upon the number and persistence of the organisms, calculating that in one case 170 million of bacilli were present in one cubic centimetre of the urine; persistence of the bacilli for three months after convalescence was seen in one case.

Smith found bacilli in three of seven cases and confirming Neumann's observations, adds that it is often possible to detect the organisms in the freshly-voided urine.

Richardson's investigations are perhaps the most important. In two series of thirty-eight and sixty-six cases of typhoid

fever, bacilli were obtained from the urine in nine and fourteen instances; the time of appearance, the persistence and disappearance of the bacilli, the coincident condition of the urine, and therapeutical resources for removing the organisms are fully discussed.

The results obtained by the above observers may be thus briefly tabulated:

1. In quite a high percentage, perhaps from twenty to thirty per cent. of all cases of typhoid fever, typhoid bacilli may be present in the urine.

2. When present they are usually in pure culture, often so numerous as to make the freshly-voided urine turbid and may then be detected by a coverslip examination.

3. Appearing generally in the second and third week of illness, the organisms may persist for months or years, probably multiplying in the bladder, the urine being apparently a suitable medium for their growth.

4. Though often showing evidences of cystitis, and marked renal involvement, the urine containing bacilli has usually only the characteristics of an ordinary febrile urine; the presence of bacilli has no prognostic importance, and their disappearance or persistence without having induced local change is the rule.

5. Lastly, as shown by Richardson, irrigation of the bladder with bichloride of mercury, and the internal administration of urotropin, a compound of ammonia and formaldehyde, seem to be safe methods of removing the bacilli; thirty or sixty grains of the latter quickly removing all bacilli in six cases.

In discussing the conditions under which bacilli may be present in the urine, it must be mentioned that an association of bacteriuria with the typhoid roseola was early noted and has been mentioned by most observers. Konjajeff held that bacteriuria indicated always the presence of the lymphoid nodules in the kidneys; according to Borges some impairment of the renal tissue was always necessary to allow passage of bacteria; Wright sees in the bacteriuria and roseola clear evidence that typhoid fever is a general infection; Blumer thought that occasionally the bacilli came to the bladder through the anterior rectal wall; Futterer's work showing the almost immediate appearance in the gall-bladder and urine of organisms injected into the portal and jugular veins, together with the fact that many urines containing bacilli show no evidences of renal changes, may be taken as indicating that the typhoid bacilli may appear in urine as a simple excretion from the blood. That typhoid bacilli are present in the blood in practically the same per cent. as in the urine is seen from the work of Kühnau and others.

Since Blumer's investigations in 1895, no bacteriological examinations of typhoid urines have been followed in this hospital. The occurrence of several cases of cystitis in the typhoid cases, and the outbreak of a small house epidemic of typhoid fever drew our attention thereto; although in the first case examined aspiration of the bladder was resorted to, it was found that cleansing the meatus and anterior urethra with 1-50000 bichloride sufficed to give pure cultures in almost every case, the standard tests for differentiating the typhoid bacillus were employed; if on examination of the fresh specimen no organisms were to be seen, as much as five to ten cubic centimetres of urine were plated out.

In most of our cases pyuria and signs of bladder irritation were present, the development of which led to the bacteriological examination; in others the urinary condition aroused no suspicion.

Case I, for the report of which I am indebted to Dr. Cushing, was at once the most remarkable and interesting, presenting a chronic cystitis of four years' duration, following shortly after an attack of typhoid fever. Pure cultures of typhoid bacilli were obtained on aspiration of the bladder; the patient left the hospital much relieved by bichloride irrigations. Unfortunately we have not been able to follow the further history of this case. Houston reports a somewhat similar case of three years' duration.

Case II showed the development of an acute cystitis at the end of a relapse six weeks from the onset of his illness; typhoid bacilli in large numbers were obtained in pure culture from the urine; the pyuria and symptoms cleared up on irrigation (bichloride of mercury 1-50000) and at present, three months after discharge, urine is quite clear and, on culture, negative.

In Case III, an outside case; marked pyuria in the third week together with the fact that the patient had never given a Widal reaction induced the physician to have cultures taken from the urine; the examination of the fresh urine showed myriads of motile bacilli, proving on culture to be typhoid; the urinary condition improved on bichloride irrigation, and three months later the urine was clear and showed no bacilli on culture.

Case IV developed pyuria in the fifth week of his illness. Numerous bacilli were present in the fresh urine; the urinary condition cleared up on bichloride irrigation; patient could not be followed after his discharge.

In Case V, the development of a cystitis three months after an attack of typhoid fever; typhoid bacilli were present in abundance in the fresh urine; the condition improved on irrigation and an examination three months later showed the urine clear and no bacilli.

The three next cases we could follow more closely, and could also watch the effect of urotropin on the bacteriuria.

In the first of these a severe nephritis and cystitis had developed in the third week of illness; the freshly-drawn urine was turbid from presence of pus and innumerable bacilli; it could be calculated in this case that 500 million typhoid bacilli were excreted in each cubic centimetre of urine.

Urotropin grs. x three times daily was begun and in two days no bacteria were to be seen in the urine, ten colonies of typhoid bacilli however growing on culture from one cubic centimetre; the nephritis and cystitis improved and after 5 days no bacilli could be cultivated; cultures remained negative for two weeks and the urine was now free from all traces of nephritis or cystitis. At this time however although patient was still taking urotropin, and after six hundred and thirty grains had been administered, typhoid bacilli reappeared in considerable numbers.

In the second of these three cases pyuria and signs of cystitis developed in the third week of illness, numerous bacilli were to be seen in the turbid fresh urine, which bacilli, though the

patient had never given a Widal reaction, proved to be typhoid organisms; after 80 grs. of urotropin grs. v three times daily the bacilli disappeared and pyuria improved, but in spite of the fact that urotropin was continued, both bacilli and pus reappeared on the eleventh day of treatment, or after 165 grs. of urotropin had been given. Treatment was continued, and in six days more bacilli disappeared entirely, and have never reappeared. In this patient it was calculated that 3 million typhoid bacilli per cub. centimetre were being excreted at the time of first examination.

The last of our cases, one of typhoid septicaemia, running an irregular course with intermittent fever and chills, and one in which the Widal reaction was at first uncertain, had nothing in the urine to attract attention, there being but a trace of albumin and slight turbidity. The turbidity was found to be due to innumerable typhoid organisms. Urotropin grs. x three times daily reduced the number of organisms to one hundred per cub. centimetre in four days. The patient died on following day still showing few bacilli in the bladder. Typhoid bacilli were found everywhere throughout the body at autopsy and in the blood before death; till the appearance of a marked Widal reaction the urinary condition in this case gave the only reliable indication of the nature of the illness, and it seems reasonable to suggest that in cases where the Widal reaction is delayed a bacteriological examination of the urine should be made, especially since it has been repeatedly shown that with the presence of the typhoid bacillus in the blood, the serum reaction may be long delayed or feeble. This absence of the Widal reaction with presence of bacilli in the urine was noted in two of the foregoing cases. As most of our cases were selected for examination on account of their urinary condition we cannot use them to figure percentages of results. In a later series of seven cases positive results were obtained in the three final cases above recorded, or in 42 per cent. of cases.

We were not able to determine at what time the bacilli appeared in the urine, their persistence for four years in one case and three months in another being seen. In the latter case the urine showed nothing suspicious till the development of cystitis at the end of three months; this patient during convalescence probably excreted millions of bacilli daily, and might have continued so to do had his urine not come under observation; estimating, as in one of our cases, 500 million bacilli per cubic centimetre of urine, a daily amount of 1000 cc. of urine would contain 500,000 million organisms. According to Petruschky's calculation, such a urine if diffused in ten cubic metres of water or sewage would give 50,000 colonies of bacilli per cubic centimetre of the water. In most of our cases there was pyuria; albumin was present twice in large amount, usually however, only in traces, with albumin generally a few hyaline and granular casts; in one case the urine showed no pus and neither albumin nor casts; complete repair of the affected bladder or kidneys, as far as could be seen from the urine, was the rule, the cystitis of four years' duration had been untreated and had become very chronic.

The observation of Neumann that in typhoid fever cloudy, freshly-drawn urine acid in reaction could usually be suspected, was frequently confirmed, the possibility of detecting the bacilli in the fresh specimen as emphasized by Smith, being shown in all but one case. For the removal of the bacilli, bichloride irrigations (1–50000) were completely effective in three of five cases which could be followed; 165 grains of urotropin removed the bacilli in one case; in another reappearance of the bacilli during its administration was seen; in a third there was immediate reduction of the number of organisms, the death of the patient preventing further observation.

The infected urine could be readily rendered sterile in half an hour by the addition of an equal volume of 1–40 carbolic acid.

Since typhoid bacilli are present so frequently and in such abundance in the urine, unless a systematic bacteriological examination can be made, all typhoid urines should be disinfected before being thrown out; great care should also be exercised in the handling and routine examination; careful centrifugalization of urine is usually possible and in the absence of cultural tests should be insisted upon; detection by this means of bacilli in fresh urines, should suggest the applicable anti-bacterial treatment and proper disinfection of the urine.

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Discussion.

Dr. Harris.—We are greatly indebted to Dr. Gwyn for this painstaking work in regard to the very important question of the elimination of typhoid bacilli through the urine. It is remarkable that as long as the organism has been known to be so very ubiquitous more examinations have not been made heretofore of the urine. The necessity for examinations of the urine as a matter of routine in all cases should be strongly brought forward. I would like to ask Dr. Gwyn some questions regarding his methods of procedure. Were dilutions made, or were plates made straight from the urine; and secondly, was any attempt made to exclude the so-called pseudo-organisms? In some of our analyses we have met with an organism that gave the reaction of the typhoid bacillus in all culture media, except in gelatine which it slowly liquefied, and even there it would be from ten to fourteen days before

it would show this difference from the typhoid bacillus. With the dry blood method it always gave a pseudo-reaction, that is, an imperfect clumping, which in a hasty examination might be mistaken for the action of the typhoid bacillus. I would also like to ask if he has tested the Hiss media, which is said to far surpass Elsner's in respect to efficiency.

As regards the lurking of the organism in the bladder for so many years is it not possible that the patient may be re-infected and a nephritis or cystitis set up by the second invasion without any of the usual symptoms of typhoid? Bearing upon my question there was a case I believe in the hospital last summer in Dr. Young's service where he credited the patient with carrying the organism for seven years. He isolated the organism and permitted me to go over the work and it was evident that he had obtained the bacillus typhosus; but he had great doubts as to whether the patient did really suffer with cystitis all the years after the primary infection.

As regards the finding of the organism in the urine I would like to know whether it has been isolated at any time in the absence of albuminuria, cystitis, or symptoms of nephritis. There are cases on record in which the urine has been reported as completely free from evidences of bladder or renal involvement; practically always, however, slight traces of albumin are found with few casts. These are matters I think that would make the routine examination of the urine very necessary. The disease may be spread, especially in country families, through the friends attending the patients and then going about ordinary household duties, neglecting the disinfection of urine and faeces of the patients, and of their own hands.

Dr. Gwyn.—I would say that in many of these cases a dilution was not necessary. As to the tests for differentiating the typhoid bacillus the usual tests, the growth in ordinary media, the motility of the organism, the non-production of indol and especially the serum test, were always used. We have not used Hiss's media this year, but I have used it before with satisfaction. In many cases the urine will show quite large amounts of albumin with casts and pus; evidences of acute nephritis and cystitis. In the majority of cases a mere trace of albumin with few casts and little or no pus will be found. Cases are reported in which the urine has shown absolutely no evidence of changes, either in the kidneys or bladder. All of our cases have shown at least a trace of albumin.

The first case I referred to is, I think, that which was under Dr. Young's care.

A CASE OF GENERAL INFECTION BY THE DIPLOCOCCUS INTRACELLULARIS OF WEICHSELBAUM.

By N. B. Gwyn, M. B., *Assistant Resident Physician, Johns Hopkins Hospital, Baltimore.*

The diplococcus intracellularis meningitidis, now recognized as the causative agent of cerebrospinal fever, while found in the meningeal lesions, has not as yet been demonstrated in the general circulation, nor have we known it to play the part of a general infective agent. During the past few months there have been admitted to Professor Osler's wards a series of 11 cases of cerebrospinal fever, and in one of these the specific organism has been demonstrated not only in the meningeal lesions, but in the blood and in the inflamed joints. The history of the case is as follows:

Jacob B., aged 24, native of the city, was admitted November 4, 1898, supposed to be suffering from typhoid fever. The patient was a packing-clerk in a manufactory, and had always been strong and well. There was no history of contact with any cases of meningitis. On Nov. 1, after two or three days of slight indisposition, the patient was seized with severe pain in the back of the neck; subsequently he had a chill with nausea, vomiting, and fever. On Nov. 2 he was very much worse. He had become delirious and was feverish. He had diarrhœa, and friends noticed that there were "drawing" movements of the hands. There was no retraction of the neck nor any stiffness of the muscles. On Nov. 4 he was seen at home by Dr. Hastings. The temperature was 100.8°; he was delirious; the limbs were very rigid; the spleen was palpable, large, and firm. He was ordered to be sent at once to the hospital. The condition on admission was as follows:

He was a well-nourished man; the cheeks were flushed, the pupils dilated, equal, reacting to light and on accommodation. He was unconscious and could not be roused. The tongue was coated; the throat was clear. The rigidity of the muscles of the neck and back was marked, and the body could be lifted with the hand placed under the occiput. The respirations were quick and jerky and there was impaired resonance in the right axilla. The pulse was 140, temperature 100.2°, respirations 44. There were swelling and redness of both elbows, the right wrist, the right knee, and several of the smaller joints of the hands.

On Nov. 5 he remained in much the same condition, with marked rigidity of the neck and of the abdomen. Purpuric spots developed about the feet. The defective resonance over the right lower lobe of the lung increased, and was present also in the left infrascapular region. The affected joints were more swollen and red. Slight external strabismus had developed. A reddish purple mottling of the skin of the body and extremities was noted. The urine contained a large amount of albumin with hyaline and granular casts and red blood corpuscles. The patient gradually failed and died at 10.40 on the morning of the 6th, the temperature having gradually risen to 105.5° before death. The leucocytes increased from 17,000 per cubic mil. on admission, to 37,000.

Lumbar puncture was performed on November 5, and cultures were taken from the blood and from the swollen and inflamed right knee joint. By the lumbar puncture a rather characteristic seropurulent exudate was obtained. In it the characteristic hemispherical diplococcus was found, both in the leucocytes and lying free, isolated, and in small clumps. Numerous large swollen forms were also seen, all of these readily decolorized by Gram's stain. Cultures from the meningeal exudate were made by inoculating the surfaces of Loeffler's blood-serum and glycerin-agar tubes with a large quantity, as much as one-half cc. After 18 hours in the thermostat at 37°C., the blood-serum and glycerin-agar tubes

showed a characteristic growth—small, isolated colonies from ¼ to 1½ mm. in diameter, on the Loeffler's blood-serum, raised, soft, viscid and white, on the glycerin-agar, rather translucent, the colonies, as seen by the microscope, being finely granular with regular borders. Morphologically the organisms showed typical biscuit-shaped or hemispherically-shaped cocci, arranged as diplococci, staining well with gentian violet, better with methylene blue, and decolorizing readily by the Gram stain.

From the knee joint about 3 cc. of thick, yellow stringy pus was obtained. Hemispherical diplococci, both intracellular and extracellular, were found in it, corresponding in morphology to those found in the meningeal exudate. Of the plates taken from the knee-fluid the blood-serum agar showed numerous small colonies about ¼ mm. in diameter, the agar plates showing also nine or ten smaller ones. The organisms were identical in form and staining reaction with those from the meningeal exudate.

The Blood. 10 cc. were taken. On the blood-serum agar plates three minute but well-marked colonies grew. They presented the typical hemispherical cocci easily decolorized by Gram's stain. In a tube of undiluted blood at the upper end of the clot which had formed, there was a faint, greyish patch, in which were diplococci similarly arranged and of similar staining reaction. In all of the cultures there were found occasional, deeply-staining, large, swollen diplococci, and others again which remained pale among the neighboring well-stained organisms.

Further cultures from the knee and blood gave typical growths on Loeffler's serum. The cultural peculiarities of the organisms from the three sources were identical and are as follows: on agar, faint growth of isolated, small colonies; in litmus-milk, no change noted, no coagulation, no acidification; growth was proved by reinoculation from the litmus-milk tubes. In bouillon, a slight cloudiness with a stringy precipitate. On potato (slightly acid) there was no visible growth, though the organisms could be demonstrated on coverslip. In gelatin and glucose-agar there was a very slight, disconnected growth, with no evolution of gas in the latter, nor liquefaction of the former.

Transplants from the undiluted blood tube gave no further growth.

In all the protocols the characteristic diplococcus, decolorizing by Gram, could be demonstrated. The feebleness of the growth of the organism was shown by the number of inoculated tubes which remained sterile, and in the fact that after 48 hours on a culture-medium reinoculation frequently gave negative results. The morphological and cultural qualities show that the organism from the three sources was identical, and was the diplococcus intracellularis meningitidis or meningococcus.

This is believed to be the first instance recorded in which general infection or septicæmia has been demonstrated in this disease. In the report on epidemic cerebrospinal meningitis Councilman, Wright, and Mallory make the statement that "so far as can be learned from cultures of blood, liver, spleen, and kidneys, at the post-mortem, septicæmia is never produced. The organisms may have been present and not grown out on cultures. They are never found except in connection with the lesions of the disease."

The autopsy on this case showed the organisms only in the characteristic lesions in the brain and cord. No serum-reaction could be demonstrated. Of special interest is the fact of the separation of the organism from the inflamed joints, which throws light upon the cause of the arthritis, not infrequently associated with the acute infections, and particularly with cerebrospinal fever.

CORRESPONDENCE.

A PIN IN THE APPENDIX VERMIFORMIS.

MAY, 1, 1899.

Editor of the JOHNS HOPKINS BULLETIN, *Baltimore.*

Dear Sir.—In your issue of January, February and March, there is an article by Dr. Mitchell on foreign bodies in the vermiform appendix with special reference to pointed bodies. I was not aware that these cases were so rare.

I reported such a case to the New York State Medical Journal, Oct. 24, 1896. In this instance the appendix had ulcerated and perforated; nature had taken care of the condition with adhesions. After the appendix was removed we found a pin in the appendix, head down, with the point caught in the wall. Upon inquiry later the little fellow said he had swallowed a pin about a year previous while playing with his brother, who tried to take it away from him, and he swallowed it to avoid his brother getting it.

Yours very truly,

D. C. MORIARTA.

511 Broadway, Saratoga Springs, N. Y.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Monday, February 6, 1899.

A Demonstration of Intestinal Anastomosis by Means of a New Forceps.—Dr. ERNEST LAPLACE.

Mr. President, Ladies and Gentlemen.—Allow me, if you please, the privilege of expressing my great appreciation of the honor conferred upon me in being allowed to appear before the Medical Socicty of the Johns Hopkins University. It is a compliment, perhaps the greatest one that a member of our profession can have at present, because of the credit which the Johns Hopkins University has brought to the profession of medicine in America. This is only appreciated by those who have traveled over this country and abroad and learned of the standing of your members. Therefore when I realize that I am with you to-night I find it impossible to express my true feelings and I can only hope that you will think me sincerely thankful for the privilege of being here.

The object of this demonstration is to show an instrument that has for its purpose the facilitating of the operation of

anastomosis. Without entering into a consideration of the operations done heretofore for this purpose, all of which have their advantages and, of eourse, some disadvantages, I believe it is agreed among surgeons that the ideal operation is that performed by means of sutures, that operation by which the ends of the gut are sutured together, and it matters little whether we use a eontinuous, a Lembert or other suture. The suture operation is the operation of to-day, and I believe is destined to be the operation of the future. Any apparatus, any instrument, any contrivanee that can facilitate the accomplishment of this operation is, I believe, something to be studied and if it possesses any merit, something to be adopted in sueh cases as require rapidity. We know that rapidity in operating will diminish the amount of shock, and may, perhaps, remove the last straw that would have broken the eamel's baek.

Now I have been trying for some time to devise these simple forceps which consist only of two ordinary hæmostatic foreeps, bent or eurved at the end into a semieircle so that placing the two together they form a complete ring or eircle. Then I have a little elasp here whieh holds them together. Now these two rings are to subserve the same purpose that the Murphy button or the Halsted rubber bags do, or that any other support within the gut ean aecomplish and in addition, no matter what stiteh you use, these rings can be removed just before the last stiteh is placed, without any difficulty.

I shall now demonstrate the manner of operating on the intestines which we have here. Inasmuch as we have to deal with intestines of different caliber we have devised five different sizes of the forceps as seen here. The smallest is for work on the gall-bladder, and it makes a quick way of operating.

I have here a stomach and a bit of intestine and my purpose shall be to unite the gut to the stomach. Putting them side by side in this way, I take the knife, and, depending upon the size of forceps I wish to use, I make the ineision. Here I shall make a large one and use the large ealiber forceps. Making the ineision directly into the stomaeh and then one into the gut I have here the two openings, into one of whieh I introduee one blade of the forceps, and into the other the second blade and they are ready to clasp. Now when this is done the operation is praetieally over. All I have to do is to put the stitches in.

Now as I go around the gut towards the end of the area to be sutured I reaeh that part of the operation whieh is ordinarily diffieult to perform. Here, however, my assistant will simply turn the forceps over, reverse the whole thing for me and, as he brings the unsutured portion of the gut before me, what has heretofore been so difficult, is now the easiest part of the operation. Now I have sutured it all around, except where the handle of the instrument projects throngh the wound and I want to remove it. I first remove the elamp, which allows the two halves of the foreeps to fall apart and then, drawing out one half, not straight, but describing a semicirele, it is easily removed and the other half ean be made to follow in the same way. Now all I have to do, is to pnt in one more stiteh and the operation is finished. I shall now make an opening in the stomach, however, and show you that the gut is perfectly patulous.

Now let us do an end to end anastomosis. Wishing to unite the two ends of the gut you first measure for the size of the foreeps needed and to make sure that the mesenteric surfaces will meet, you begin by plaeing the four fixation sutures at the four cardinal points. Now I can introduce the foreeps anywhere between these stitehes. Dr. Cushing very properly asked me to-day, "What would you do if you had to anastomose guts of different caliber?" The answer to that is that I should invaginate the two ends, and for that purpose I have devised this little instrument for catching the gut at its bordèr, dipping it down into the bowel, stitching it nearly all the way aronnd, and then withdrawing the foreeps.

Now gentlemen, this I believe meets all the possible indications for operation upon the intestines. I first presented this method at the last meeting of the American Medieal Assoeiation in Denver, last June, and on the same day it was published in the Philadelphia Medical Journal. I have since then demonstrated it in Philadelphia and other places. At one of these demonstrations I invited a gentleman in Philadelphia to see the operation, aud at its close he told me that he could simplify these forceps, and within 24 hours he exhibited the forceps he had made. His description of them was published last Saturday in the Philadelphia Medieal Journal. I wish therefore, in justice to this instrument, to say a few words, not in eriticism of his foreeps, but simply to show how they were developed. It is natural to suppose that in getting up an instrument of this kind it did not jump into existence all of a sudden; it had to grow, as it were. The idea was to have a ring that would be removable and it was natural to think first of a ring sueh as he devised instead of one like this, and in fact, the very first forceps I made had exactly the shape of that published by this gentleman last week; it was $\frac{7}{8}$ round and $\frac{1}{8}$ open. He has no claim to originality except that the forceps are simpler than mine. You can easily see that when I remove one-half of these forceps at a time I have to describe a semieircle, and if either branch of the forceps were more than a semicircle I should have to make the turn something more than a semicirele to remove it. In other words, to divide a ring into the two smallest possible portions I must divide it in half, for if one portion be smaller than a half, the other must be larger. This gentleman published his elaim 24 hours after he first thought of the idea and he therefore had no opportunity to test it, and he does not know what I learned by experience. I elaim therefore that while his may be simpler it does not meet all the requirements of the case and I have given mine the shape you see because it seems to be the simplest possible instrument that will meet every possible emergency. I have in my possession the first forceps I used for this purpose more than a year and a half ago, whieh are like those published Saturday, and whieh I discarded because it was not the required thing.

Dr. Halsted.—I should think that for a lateral anastomosis it promises all that Dr. Laplace elaims for it and we shall certainly give it a trial very soon. It is quicker, much quieker, I should say, than the method we employ; I eannot say how many minutes, because, of course, one cannot deter-

nine that point by work upon alcoholic specimens. I should think it would be of great assistanee espeeially for ehole-eysto-enterostomies. It is possible, of eourse, to do this operation without an instrument, but it is a very difficult one.

I was interested in Dr. Laplace's reply to Dr. Cushing's question as to what he would do in an end to end anastomosis if the guts were of different sizes. If I understood him he would really do a lateral anastomosis, or reduce them to the same caliber. The fact is that in surgery one very often, perhaps usually, when doing end to end anastomoses, has to deal with intestines of different sizes. I think we have had three or four within the last year where the intestines were of different size and it is a question still, I suppose, as to whether it is not advisable, if possible,—if it is not preferable I mean, to do an end to end anastomosis rather than a lateral anastomosis, because we do not, as you know, have as good ultimate results in the latter as in the former.

DR. LAPLACE.—I believe that in sueh a ease as Dr. Halsted speaks of, if the gut is distended and thin it ean be puekered up in the manner I have hinted at, that is, having made the four cardinal sutures, if the guts do not invert, all you have to do is to insert a temporary suture, pucker the large gut and then continue as you would with the Murphy button.

A New Operation for Vesico-vaginal Fistula.—DR. KELLY.

I wish to present two interesting cases whieh I have had during the past year, in whieh I have been obliged to resort to new procedures in operating upon vesieo-vaginal fistulæ. You all know very well that the history of the vesico-vaginal fistulæ instituted an important era in the history of surgery at large; in fact, I imagine the enthusiasm over the work of Jobert of France, Sims of this country, and Simon of Germany, was due to the faet that men recognized that it was the replacing of older surgery by newer and more aeeurate work. Now when Sims closed vesico-vaginal fistulæ and sueeeeded as no one had suceeeded before, and as Dr. Emmett succeeded even better afterwards, better perhaps, than any one ever will again, I think men felt that the chapter on this subject had been closed. The truth was, it had only been opened, for the operation was applicable only to the simple eases and it was neeessary to devise new operations for the more difficult cases. We know that even these operators did not sueeeed in a large percentage of cases, for in many they were obliged to resort to elosing the vagina and turning the current of the urine into the rectum.

The great difficulty in handling certain cases of vesico-vaginal fistulæ is due to two faets: in the first plaee, the fistula may be a very large one, and in the second plaee there may be such an amount of scar tissue surrounding the fistula that its resistance prevents bringing together the parts. In eases of large fistulæ with entire loss of the base of the bladder and with scar tissue in the vagina, the old method of operating was to open through Douglas' cul-de-sac, turn the uterus so that its fundus was brought out at the vulva, suture the bladder to the posterior wall of the uterus so that it was made to do the work of the base of the bladder, finally making a hole in the fundus through whieh the woman could menstruate. The most important reeent finding has been the recognition of the faet that the bladder tissue itself is not often seriously involved in the sear tissue, and that the bladder ean be drawn down and sutured to itself so as to close the fistula. This is a very important faetor in the treatment of eertain of these cases that cannot be treated in the elassical way.

A case came to me from New York this fall, upon which an abdominal hysterectomy had been performed for fibroids. There was a large fistulous opening into the bladder, from the vault of the vagina. It was very elose to the peritoneum, high up in a virginal vagina, had been operated upon several times and there was an abundance of sear tissue. The edges of the fistula were of such charaeter that I eould have no hope of bringing them together and securing union. I opened the abdomen, my intention being to expose the pelvic floor, dissect the bladder away and sew it up. The patient had a very large ventral hernia and, unfortunately for the faeility of the operation, was very fat. I opened the abdomen, started on my plan, but in attempting to separate the bladder it began to tear and tore so widely that I saw at onee a sueeessful operation as planned would be impossible. I then cut through the top of the bladder to see if I eould get at it from the inside, and then freshen and bring the edges together. I eould not do this and therefore split right down through the opening to draw the parts together, but I found that this procedure eould not be carried out satisfactorily and so I followed this plan which succeeded. The bladder was widely opened, in faet split in half; I found the bladder in front of the fistula fairly movable and I eontinued the denudation directly down, starting with the bladder walls above and then, passing some catgut sutures, bringing the wounds together. I had thrown out of use a little of the bladder at the sides of the fistula. I then put a drain through the vagina up into the peritoneum and closed up the hernia, whieh was an extensive one. The patient made an immediate and perfeet reeovery.

It is a new thing to have gone, by means of a suprapubic incision, through the mucosa of the bladder, drawn the fistula out and closed it by diminishing the eapaeity of the bladder.

CASE 2. A doetor wrote me from Virginia that he had a case of vesico-vaginal fistula and wanted to know what was the best way to operate upon it. I replied that the best way was to send it up here, as he had had no experience in operating upon such cases. The fistula could not be gotten at from below; I therefore opened the abdomen, separated the bladder, freed the fistula on both sides and brought the edges together with catgut. The result was a perfect recovery.

DR. HALSTED.—In the first case, Dr. Kelly, did you excise the portion of the bladder that contained the fistula?

DR. KELLY.—No.

DR. HALSTED.—What became of it?

DR. KELLY.—It lay up in the peritoneal cavity protected by a drain.

DR. HALSTED.—Does she still have a little fistula?

DR. KELLY.—No, it is all closed up.

Primary Cancer of the Appendix.—Dr. Hurdon.

Dr. Hurdon presented a case of primary cancer of the vermiform appendix.

Dr. Kelly.—This subject is a large one and it would require a volume to go into it completely and do it justice, so that here one can only outline a few of its important relations. I have been paying close attention to the relation of appendical disease to pelvic diseases for a long time, and the records of our department will show the exact condition of the vermiform appendix in every case in which the abdomen has been opened for about 2 years past.

We meet with appendical disease in a great variety of relationships. We may have cancerous disease of the appendix as in this case, where there was an adeno-carcinoma, which showed no relationship to the pelvic disease; then, again, we meet with cases in which the disease is dependent upon the condition of the pelvic organs. I had within 48 hours, last week, five cases in which I had to remove the appendix.

Where the disease depends upon the pelvic organs, the appendix becomes adherent to the diseased organ, as a uterine fibroid, or an ovarian tumor; these cases we see quite frequently. Then again we meet with a class of cases in which the appendical disease has followed an operation; these are more rare, but quite interesting. After a clean operation, as the enucleation of a diseased tube or ovary, the patient within a few months or a year complains of a pain in the right side, etc. The abdomen is opened and the appendix is found adherent to the seat of the former operation. I have had such a case within the past ten days, where the appendix was pulled out long, and was adherent to the old wound.

It is important to bear this in mind and always inspect the appendix whenever a laparotomy is performed.

This case emphasizes another important fact, that is, how to treat these cases by operation. I believe in the removal of all abnormal appendices, but I do not believe in taking advantage of the opportunity to remove a normal appendix.

Monday, February 20, 1899.

New use for Renal Catheters.—Dr. Kelly.

I have a brief but important communication to make regarding the further extension of the use of renal catheters.

It did seem a few months ago that certain discoveries were going to limit the use of them. Dr. Neumann, of Guben, found that without catheterizing the ureter he could separate urines and retain them separated in the bladder, obtaining them later from the bladder by means of tubes. This was done by using an instrument of this kind (drawing) which he calls a urine separator. It is a tube with a solid septum running down the centre and projecting beyond the end of the glass tube; the form of the catheter is retained by means of a wire cage. Urine running in this side will run down and discharge at the outer end, and the same for the other side. If we put this instrument into the female urethra and bladder, press it up against the symphysis and then with the index finger in the vagina, push the floor of the bladder against the instrument, we have the floor of the bladder separated into two loculi so that the urine coming out of the right ureter runs down on one side, and that from the left on the other, thus giving us a simple method without using the catheter.

This was published in October in the Deutsche medicinische Wochenschrift and not long after Dr. Harris, of Chicago, was able to use a small staff so as to form two little pockets in which the urine was accumulated and was drawn off by the catheter.

These methods did look at first as if they would very much limit the field of the catheter, but a new and very important use for the catheter has recently arisen.

We all know that some of the most obscure cases with which we have to deal are those in which there is vague but distressing pain in the side, especially the right, and one may long be in doubt as to whether the pain is renal, hepatic, intestinal or hysterical. By means of this catheter, I have been able to include or exclude the kidney. When the upper end of the catheter presses upon the pelvis of the kidney the patient will sometimes tell us that we are touching the very point where she had the pain. Further than that, I have been able to produce an attack of artificial renal colic by injecting solution of boracic acid into the kidney through the catheter. Again, a patient who has been suffering from renal colic will often have afterwards an attack of genuine renal colic following the treatment. I have had two cases recently that are interesting in this connection. In one there was a tumor below the ribs on the right side. Some five or six consultants gathered together to determine what it was, some thinking it to be a tumor of the gall-bladder. I injected fluid and the patient at once complained of pain in the back quite as severe as a genuine attack of renal colic, so we were satisfied that the kidney was in its normal position.

In the other case which occurred not long ago, the condition was so exactly like a large floating kidney that I unhesitatingly made that diagnosis, nevertheless I passed in the catheter first and produced an attack of colic. The patient would not locate the colic in the lump we felt in front but insisted that it was in the back. We then made a median incision to examine the opposite kidney. Instead of cutting posteriorly I cut in the median line and found by the hand that the left kidney was normal, but on examining the other side I found an enlarged gall-bladder in front of the kidney. The induction of the renal colic and location of the pain by the patient thus gave us our correct diagnosis.

There are then, several valuable uses for ureteral and renal catheters in the future, especially to diagnose the cause of pain, particularly in the right side.

Every surgeon must think at once of the chances of introducing infection into the higher urinary tract, and I am extremely careful about introducing catheters in a case where there is much infection.

I have never seen an infection conveyed from the lower into the higher urinary tract by catheterization of the ureters.

NOTES ON NEW BOOKS.

An American Text-Book of the Diseases of Children. By American Teachers. Edited by Louis Starr, M. D., assisted by Thompson S. Westcott, M. D. Second edition, revised. (*Philadelphia: W. B. Saunders*, 1898.)

The second edition of this work is in many respects an improvement on its predecessor. In any work, by so many authors, a certain overlapping of material and variety of opinion on important objects is to be expected, and compared with similar works by a single author, must seem lacking in uniformity. Under the competent editorial direction of the present volume, however, this defect has been as far as possible eliminated. The entire subject-matter has been revised, many articles rewritten, and some new ones introduced.

Among the latter are "Modified Milk and Percentage Milk Mixtures," "Lithæmia," and a section on "Orthopædics."

The first of these is brief but sufficiently practical for a working knowledge of the important subject.

"Lithæmia" is well discussed by Dr. B. K. Rachford. The author, however, speaks with a certainty of the rôle of the alloxuric bodies hardly warranted by our present imperfect knowledge of the pathology of the so-called uric acid diathesis.

In a short section of twenty-seven pages, Dr. J. E. Moore has condensed much of real use to the general practitioner on the subject of orthopædics. The article is well illustrated and is a decided addition to the volume.

The articles rewritten are "Typhoid Fever," "Rubella," "Chicken Pox," "Tuberculous Meningitis," "Hydrocephalus" and "Scurvy."

Those on "Infant Feeding," "Measles," "Diphtheria" and "Cretinism" have been thoroughly modernized.

In the treatment of diphtheria one expects more emphatic mention of the antitoxin and less of the use of such almost extinct measures as swabbing with hydrogen peroxide, calomel insufflations and the various solvents mentioned.

The articles on hereditary syphilis and diseases of the new-born are very good.

In the light of recent investigation more mention might be made in the articles on cerebrospinal meningitis of the bacillus intracellularis of Weichselbaum. On the whole, however, the book very well fulfills the purpose for which it was compiled—a text-book for students carefully condensed with few omissions, and a reference book sufficiently practical for the general practitioner. The mechanical construction is excellent, and the numerous illustrations instructive. R. A: U.

Text-Book of Materia Medica, Therapeutics and Pharmacology. By G. F. Butler. Second edition. (*Philadelphia: W. B. Saunders*, 1898.)

A review of this book was published in the Bulletin about two years ago. The changes in this edition seem to be very slight, the only notable additions being a table of the "untoward action of drugs" which brings a large amount of very useful information into a small compass and a form convenient for reference.

Annual and Analytical Cyclopædia of Practical Medicine. By Charles E. de M. Sajous, M. D., and one hundred associate editors assisted by corresponding editors, collaborators and correspondents, Vol. II. (*The F. A. Davis Co., Philadelphia*, 1898.)

Volume II of the Annual and Analytical Cyclopædia of Practical Medicine contains some valuable articles on therapeutics; not only are the latest papers and cases cited, but a systematic account of the preparations of the drugs and their physiological action is given; special emphasis, however, is laid upon the untoward action of the drugs and their use in therapeutics. All the most important drugs between bromide of ethyl and digitalis are discussed in this volume, and in most cases with considerable fullness. Thus 22 pages are given to chloroform and 7 to digitalis. Under chloral the various new combinations of this drug with other hypnotics are described and their relative merits discussed. Under bromine and its preparations considerable attention is given to bromism and a word of warning raised against the reckless use of these remedies in epilepsy.

Some of the other drugs discussed in this volume are cinchona, caffeine, colchicum, the preparations of copper, curare (which seems to be yielding good results in certain diseases), cubeb, etc. In some cases (notably in the article on digitalis) there is a tendency on the part of the editor to quote freely from the ordinary text-books on the subject rather than from original papers, but on the whole perhaps the most recent views of physicians as to the value and methods of administering the drugs which are discussed in this volume are nowhere better expressed than here.

Essentials of Materia Medica, Therapeutics and Prescription Writing. By Henry Morris. (*Philadelphia: W. B. Saunders*, 1898.)

This useful little book has now reached its fifth edition. The general plan is the same as in former editions, the chief alterations being the omission of certain parts and the introduction of some of the newer remedies. Welcome additions are the introduction of the metrical, as well as of the apothecaries' system of weights and measures, and a very carefully prepared index. It seems to us that this little work has more value than some of the numerous manuals which though more pretentious are neither fuller nor more accurate.

Saunders' Pocket Medical Formulary. By W. M. Powell. Fifth edition. (*Philadelphia*, 1899.)

This book contains over seventeen hundred prescriptions arranged alphabetically according to the diseases to be treated; these formulæ are taken from a great variety of sources—text-books and manuals of therapeutics, medicine, surgery, obstetrics, the various specialties, from original papers, and not a few from various hospitals. The book also contains tables of doses, incompatibles, antidotes, gargles, inhalations, a "surgical remembrancer," a diet table, obstetrical tables, etc., all arranged in such a way as to make consultation of it as easy as possible. It is remarkable how much information the author has succeeded in getting into so small a book.

The Anatomy of the Central Nervous System of Man and of Vertebrates in General. By Ludwig Edinger. Translated from the Fifth German edition by Winfield S. Hall, Philo Leon Holland and Edward P. Carlton. 445 pages. 258 engravings. (*F. A. Davis & Co., Publishers*, 1899.)

Great productive activity has characterized of recent years the study of the anatomy of the nervous system. Even the investigator devoting his whole time to the subject finds it almost impossible to keep thoroughly acquainted with the results of others in the same field, and any text-book grows old so fast that revised editions of it appearing only a few years apart, have to be so much rewritten as to seem like new books.

The two authors who have been most successful in seizing from the great mass of ideas and facts annually brought forth materials wherewith to build clear and definite representations of modern neurological conceptions are Van Gehuchten of Louvain, and Edinger of Frankfort. The former writes mainly from the point of view of outline schemes based upon the neuron concept. Edinger, on the other hand, while utilizing both the neuron doctrine and outline schemes, is concerned rather with the form relations of the anatomical mechanisms of the nervous system. His illustrations have, many of them, the rare merit of suggesting real structures and the third dimension. He has been especially interested in comparative studies. In the preface to the second edition, quoted in the fifth, he writes as follows:

"There must be a number of mechanisms which are present in all vertebrates: those which make possible the simplest expressions of the activity of the central nervous system. It is only

necessary to find that animal or that stage of development in any animal in which this mechanism appears in so simple a form that it may be completely understood. Once any one has anywhere perfectly established the relation of such a mechanism, *e. g.* a nerve bundle or a cellular structure, he is able usually to find it again, even where, through adventitious matter, it is made more or less obscure. The discovery of such fundamental features of brain-structure appears to be the next and most important task of brain morphology. Once we know them it will be easier to understand the complicated mechanisms with which the more highly organized brain performs its function."

The suggestiveness of this point of view, together with a clear and attractive style have rendered Edinger's book deservedly popular. Successive editions have rapidly followed one another, the first, quite a small volume, appearing in 1885, the fifth, greatly enlarged, in 1896. The book is now divided into three parts.

Part I is introductory. In forty pages a clear, interesting and concise description of the fundamental ideas accepted by most modern neurologists, is given.

Part II gives a review of the embryology and the comparative anatomy of the vertebrate brain. Something over 100 pages are given up to this subject. It is especially attractive because of the author's personal researches in this line.

Part III treats of the structures found in the mammalian, especially in the human brain. To this nearly two-thirds of the book is devoted. Text and illustrations serve to make this intricate subject uncommonly clear.

The translation is for the most part fairly satisfactory. The illustrations have been well reproduced. The book should meet with the welcome reception it so richly deserves. B.

The Pocket Formulary for the Treatment of Disease in Children. By Ludwig Freyberger, M. D., Vienna. M. R. C. P., London. M. R. S. C., England. (*Rebman Publishing Co., London*, 1898.)

As is stated in the preface the object of this little book is to give the busy practitioner and senior student of medicine, in a concise and handy form, all of the information which may be required as regards the treatment of diseases of children by drugs.

The greater part of the work is taken up by a list of remedies, arranged in alphabetical order, which are best suited to the treatment of children's diseases, and each drug accurately but briefly described as to its properties, source and dose. The scheme which has been adopted in the discussion of the various remedies is as follows: Properties, under which are mentioned the source, ingredients, methods of preparation, etc.; Use, whether internally or externally, and for what; Therapeutic dose, in both English and French (metric) system; Incompatibilities, Correction of Taste, followed by one or more formulæ which, in the author's opinion, are the most suitable modes of administration of that particular drug. The Appendix contains formulæ for sprays, gargles, hypodermic injections, enemata, and suppositories, and the Therapeutic index, which completes the volume, contains an alphabetical list of the diseases of infancy and early childhood, together with the special remedies, which are indicated in each affection.

The book is of a convenient size and of suitable binding to be carried in the pocket, and cannot fail to fulfill the mission for which its author has put it before the profession.

A Text-Book of Mechano-Therapy: by Axel V. Gräfstrom, B. Sc. M. D. (*Philadelphia: W. B. Saunders*, 1899.)

This little book is designed for the use of medical students and trained nurses. There is a strong need for a concise presentation of this subject. In part, it is well supplied here. The book throughout is dignified in tone. Its average merit is more than fair, but its execution is unequal, and many details are open to criticism.

The work treats of both Medical Gymnastics and Massage. A synopsis of the Swedish movement system constitutes the first division. The classification here is especially to be commended and stands in contrast with much of the discursive and sometimes bewildering literature of this subject. The movements are graphically described, and with or without practical demonstration will serve as a competent guide or reference book to the student. It is to be regretted that in the second division of the book, which relates to Massage, the nomenclature which has become classic through use in the best schools and by the best writers, has been abandoned. Further, while it is of course impossible to master the detail of technique from text-books only, the chapter which treats of it will be little help to the novice. The illustrations of a patient's position while undergoing a kneading of the abdomen is, indeed, distinctly incorrect. At most it can be said that there is furnished here a working basis solely for teachers. The chapter on General Massage is negative, and falls short of the requirements of teachers or scholars. There should be outlined, as was shown to be possible in the Swedish movement system, a definite and recognized system of massage—like that of Dr. S. Weir Mitchell, or of the Swedish or the German school. This outline should include directions as to the position of the patient and of operator; and something of the action of the hand and of its relation to the presented surface.

The concluding chapters, which treat of the application of mechano-therapy to the treatment of disease, aside possibly from the omission of some practical suggestions, are exceptionally thorough, although necessarily and intentionally condensed.

It is interesting to find here included, among the applications of mechano-therapy, the treatment of hernia by taxis, and the kneading of the uterus after labor to maintain contraction—all legitimate forms of massage and very properly so considered.

Foundations of Zoology. By William Keith Brooks. A course of lectures delivered at Columbia University, on the Principles of Science as illustrated by Zoology. (*New York: Published for the Columbia University Press by The MacMillan Co.*, 1899.)

The theme of most of the thirteen lectures is the nature of life which, rather than the physical basis of life, is held to be the foundation of zoology. Huxley's statement that protoplasm is the physical basis of life, leaves out of account the essential idea of fitness as an attribute of such a basis, and the nature and origin of this fitness form the subject of a large part of the discussion.

The author in approving Spencer's definition of life—the continual adjustment of internal to external relations—elaborates it by considering in more detail the nature and effect of external relations or environment, all of which he includes in the term "nurture." "Life is response to the established order of nature." In nature each stimulus which may call forth a response is a sign with a significance, and life is the use of the ability to read and act on these signs—to read the language of the environment.

From this he passes on to show that the nature of the response depends on what, in the experience of the ancestry was found beneficial, and here he develops in an interesting way a reconciliation between the opposing ideas that the development of the complicated nature of an organism with its ability to respond to stimuli is due on the one hand to the inherent potency of the germ, or on the other to response at each stage of its embryological development to external stimuli, by the idea that were we to know exhaustively the nature of the germ, we might see that the responses made to the external stimuli were no more than, from the nature of the germ, we might expect. From all this it is plain that the beneficial result of interpretation and response to stimuli depends on whether the stimuli or signs have the same significance as they had in the time of the ancestors.

These ideas are based on the essential conception that those

animals which do not respond to stimuli properly, in the end die out, and the ability to respond is continued from one generation to another, not by the inheritance of the results of individual adaptation, but by the inheritance of the adaptive mechanism, which is in the end the object of the selective process. Do we exaggerate the importance of the adaptive mechanism when we say that we acquire no nurture except that which our nature provides for? Life is, perhaps in each invidual case, an acquired art, and the adaptive mechanism the inherited thing, and the basis of our expectation of what the organism will do under certain stimuli. In other words, except for the guiding influence of the adaptive mechanism, the influence of nurture will be fortuitous in its effects.

It seems to appear from this that as physical modification is, in the end, dependent on the function demanded for the existence of the species, the adaptation must occur in the active relation to environment, *i. e.* the response to stimuli, and this response depends on the adaptive mechanism which is inherited and competent as long as the environment is essentially that for which in the ancestors the adaptive mechanism was prepared by selection. As soon as this environment changes selection must again intervene and modify the adaptive mechanism.

The views of the Lamarckians are discussed with no great forbearance, and their absurdity especially brought into relief by the idea that "the probability that haphazard effects of nurture will be injurious is prodigious—even if they *are* inherited, they will probably not chance to be beneficial independently of selection—the chances are, therefore, against adaptive modification by the direct action of the environment."

The effects of nurture are to be distinguished from those of ancestry, and here there is introduced an interesting conception of the genealogical tree; for while most writers speak of a geometrical progression in the increase of ancestors, as we go further and further back, Prof. Brooks shows that these diverging lines, after a little, essentially converge, and that if we go back far enough the plan of ancestry of an individual is rather like a long thread with frayed edges, and from this he deduces the origin of a species from a very few individuals—perhaps one, whence the origin of genera from individuals, and of the metazoan from one protozoan. He pictures the development of the individuals of the bottom fauna from the pelagic in the ancient ocean—their growth in size and powers, so that they subsisted on their ancestors, and traces the peopling of the earth from these. Even to-day the existence of animal life in the sea is still ultimately dependent on the most minute pelagic creatures, which form their food. He gives a most vivid account of the tropical marine fauna, impressing on us the extraordinary absence of vegetable life in those depths, and the fierceness of competition in the bottom fauna as compared with the pelagic—the larvæ of animals living on the bottom become pelagic in the deeper part of the ocean, because otherwise they would be devoured by their parent's neighbors.

The author goes on to the discussion of the argument from contrivance in creation as opposed to the evolution of beings—the consideration of the teleological explanation of creation. As to the "eternal paradox about necessity and freedom he, as an humble zoologist, who admits his accountability, is quite content to leave to Milton's fiends the discussion of 'Fixed fate, free will, foreknowledge absolute.'"

As to the manner of the creation he attempts a reconciliation of the views of Darwin, Gray and Huxley in the wider teleology of Huxley. He does not wholly agree with Huxley in considering that the argument of Paley that the contrivances of human artificers prove nature a contrivance and the work of an artificer has received its death blow in natural selection, but thinks that Paley's argument is rendered inconclusive.

The lectures are concluded with a consideration of the work of Agassiz and that of Berkeley. Agassiz's idea of the wider teleology—that "it is not because we find contrivances in nature, but because the order of nature is one consistent and harmonious whole that he holds it to be intended"—was, of course, pre-Darwinian. He considers all the data of natural science as a language in which the creator tells us the story of the creation, and Berkeley too, finds in the signs to which in life we learn to respond, as stimuli, the parts of a language which we come unconsciously to read and know—in which the creator reveals to us the intentions of the creation.

The book is interesting in its breadth of conception and clearness of style. While in the main a criticism of the theories expressed by previous writers many of the theses are based on the profound knowledge of biology of the writer himself, and we cannot but think as we follow his convincing reasoning, that we have before us the latest addition to American classics in scientific literature. W. G. M.

The Mineral Waters and Health Resorts of Europe. Treatment of Chronic Diseases by Spas and Climates, with Hints as to the Simultaneous Employment of Various Physical and Dietetic Methods. Being a revised and enlarged edition of "The Spas and Mineral Waters of Europe." By Hermann Weber, M. D., F. R. C. P., and F. Parker Weber, M. D., F. R. C. P. With a map. (*London: Smith, Elder & Co.*, 1898).

The title of this enlarged and revised edition of a well-known work, states in a general way its scope and purpose. It is, however, more than a mere description of the various European sanatoria; it includes a general account of the therapeutic uses of water that, in itself, will be found a valuable guide to the many who wish to utilize this agency. The usefulness of health resorts, as the authors claim, is not overstated, and all the accessories to the water cure are fairly stated and valued; it would be a very excellent thing had we some work of this kind on American health resorts.

Two new chapters have been added, besides the general revision; one on sanatoria other than hydropathic ones, and one on the different diseases in relation to the selection of mineral waters, climatic and other cures, etc. The latter is quite lengthy and full; the former hardly as much so as it might well have been made, or as the subject deserved. Considering the importance attributed to it at the present time, the space given to sanatoria for consumptives, (*only* about four pages), is not by any means as much as could well have been devoted to it. There is already quite a growing literature of the subject, and it seems likely to have a larger share of professional and other attention in the near future.

The bibliography at the end of the book, though not exhaustive, is quite lengthy, and will be found useful for reference.

Atlas of Syphilis and the Venereal Diseases, including a brief Treatise on the Pathology and Treatment. By Prof. Dr. Franz Macek. English translation from the German. Edited by L. Bolton Bangs, M. D. Seventy-one colored plates. Cloth, $3.50 (*Philadelphia: W. B. Saunders*).

This admirable little volume deserves a wide circulation. The full page colored plates, from original water colors, are remarkably well-executed for a work of such popular price. The various manifestations of syphilis are taken up in order of their development, and together present a vivid pictorial representation of the disease. The lesions of chancroid, bubo, condylomata, etc., are given much less space, but are well shown. The appended treatise, while necessarily brief, is only fairly well done, and the methods of treatment are not such as would find favor in this country. To treat syphilis solely by inunctions which are discontinued almost as soon as a disappearance of the symptoms occurs, and only resumed in their reappearance, seems to us irrational, as well as dirty, and tedious. Since the author omits the protoidid from

the preparations of mercury used in syphilis, and remarks that the "best way is to give the patient a bottle of potassium iodid and let him *prepare it himself*," we are not surprised at his failures in the internal treatment of syphilis. H. H. Y.

The Office Treatment of Hemorrhoids, Fistula, etc., without operation, together with remarks on the relation of diseases of the rectum to other diseases in both sexes, but especially in women, and the abuse of the operation of celostomy. By CHARLES B. KELSEY, A. M., M. D., etc. (1898, *E. R. Pelton, N. Y.*)

The title of this little book would lead one to suppose that some new and simple method of treatment is to be promulgated, and the reader is fed on glittering generalities, medical anecdotes and chit-chat, until finally a time comes for divulging the long-expected panacea, when the whole subject is dismissed with the remark that there is not time to describe the plans of treatment.

The author asserts that he prefers always a "straightforward," truly surgical operation, such as "laying open the bones for fistula," and "clamp and cautery" for hemorrhoids. All surgeons, however, would hardly agree with his idea of "straightforward" surgery. For one, we would protest against the widespread usage of such barbaric and unsurgical treatment as the clamp and cautery. The cautery was, doubtless, a valuable surgical instrument before our forefathers learned how to ligate vessels, but since that date its use has been discarded by all surgeons except the pile specialists.

It has been clearly shown by Quéme that hemorrhoids are due to a general phlebitis of the inferior hemorrhoidal plexus—around the entire anal circumference; it is evident that burning off a more prominent lobule here and there does not eradicate the disease. This is proven by the frequent recurrence or development of piles in areas not burned—that is, from diseased vessels left behind.

How representative surgeons can prefer such crude methods to the beautifully exact, radically truly surgical and absolutely curative procedure known as the Whitehead operation, it is hard to understand. To say that the latter method is difficult, hemorrhagic and tedious, is a confession of inferior operative ability.

This little volume is divided into three parts—the first being a description of that "office treatment" which eludes the reader at the last moment. The second part is an exhortation to young would-be rectal specialists to consider the broadness of their chosen specialty, and not to worry over the narrow limits of their pasture.

I will quote at length, as the line of argument is interesting as showing how a specialist entering the body at one little "locus minoris," so to speak, may gradually claim, by propinquity, and sympathy, sovereignty over the larger part of the body. It reads:

"Would any of you admit to a patient that, although your specialty called upon you to be able to operate upon an abscess opening into the bowel at one point, you did not feel competent to operate upon another opening a little higher? . . . . Are you equal to a resection of a stricture six inches up the bowel and not at twelve? . . . . Do you wish to take the position that you can suture the bowel to the skin, but cannot suture one cut end to another, that it is your business to remove tumors from the rectum which are pressing upon the uterus, but not tumors of the uterus pressing upon the rectum?

"So you will find the path of practice opens into many broad fields of study and interest, and my advice is to follow them for your own sake . . . . then you have a specialty broader perhaps than any other, and certainly affording ample scope for all of your powers of study and thought."

The last part, which deals particularly with excision of the rectum, as against colostomy, is good surgery, and reflects credit on the author, whose previous good reputation is not enhanced by the previous chapters.

BOOKS RECEIVED.

Annual and Analytical Cyclopædia of Practical Medicine. By Charles E. de M. Sajous, M. D., and one hundred associate editors assisted by corresponding editors, collaborators and correspondents. Volume III. 4to. 1899. 600 pages. The F. A. Davis Co., Philadelphia.

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THE PRESENT ASPECT OF SOME VEXED QUESTIONS RELATING TO TUBERCULOSIS, WITH SUGGESTIONS FOR FUTURE RESEARCH WORK.*

By E. L. Trudeau, M. D., *Saranac Lake, N. Y.*

Gentlemen:—I venture to say a few words to you to-day on some of the vexed questions connected with the study of tuberculosis. Any of us who can look back some twelve or fifteen years can bear testimony to the progress which has been made by experimental research in our knowledge of this disease. Viewed in the light of the past it would seem that the future is full of promise as well as of unsolved problems. It is not, however, of the past triumphs of the experimental method that I wish to speak so much as of some of the as yet unanswered questions relating to tuberculosis which confront us at every step, and on which we so greatly need light before we can hope for larger results in staying the ravages of this widespread disease. I venture, also, to make a few suggestions as to what seem to me to be the most promising lines for future work in relation to the etiology, pathology, prophylaxis, bacteriology, diagnosis and treatment of tuberculosis.

Etiology.

In regard to etiology, we need to know more as to the cause of the wide variations in the manifestations of the disease. Are these due to differences in the virulence of the infecting germ, to variations of the resisting power of the tissues, natural or acquired, or to both these factors?

What constitutes virulence in the infecting bacilli? Is it due to an increased capacity for elaborating toxins in greater quantity, or to the elaboration of more highly toxic products by the microbes, or does increased virulence depend merely on an inherent capacity of the germ to grow and spread more rapidly in the body?

In this connection I may state that, in my experience, tuberculin made from the culture fluid in which bacilli attenuated by long cultivation have grown is apparently as efficient in producing the usual tuberculin reaction in tuberculous men, and in killing tuberculous animals, as tuberculin derived from the most virulent cultures.

We need more light of an exact nature in regard to the various channels by which the bacillus gets access to the body, and in this connection it may be noted that the large proportion of cases presenting adenoid growths in the nasal fossæ which react to tuberculin would indicate that this portion of the respiratory tract is more frequently a channel of primary infection than is generally recognized.

*A Lecture delivered at the Johns Hopkins Hospital, on May 1, 1899.

What is predisposition? It may be individual or racial. Individual susceptibility may be inherited or acquired. It is, in either case, greatly influenced by all factors which tend to produce lowered vitality and imperfect nutrition, and which may be grouped under the terms heredity and environment. A susceptibility to the disease may be inherited; an unfavorable environment may precipitate infection, whereas a favorable one may avert it and even arrest and cure the disease when it has begun to develop. Racial susceptibility presents to the experimenter many curious problems for study which show that the line which divides immunity from susceptibility is a narrow one. Thus we find chickens highly susceptible to infection with the avian variety of the tubercle bacillus, while they resist inoculation with the bovine and especially the human bacillus. Indeed, so insusceptible are they to the human bacillus that they resist feeding for months on tuberculous sputum, and I have made repeated intra-peritoneal inoculations of large quantities of the most virulent cultures of human bacilli in a great number of chickens without the slightest deterioration in health resulting, and these birds when autopsied showed no trace of the injections or any evidence of disease in any organ. The guinea-pig, on the contrary, succumbs readily to inoculation with human bacilli, and is killed even more quickly by the bovine variety, but resists injections of avian cultures, which produce generally only a local ulceration in these little animals. The rabbit, on the other hand, is killed by all three varieties of the tubercle bacillus. Some slight artificially-produced variations, however, may efface the resistance of the chicken to the human, and that of the guinea-pig to the avian bacillus. Nocard[1] has recently reported that by cultivating for some time human tubercle bacilli, enclosed in celloidin capsules within the peritoneal cavity of chickens, he could obtain cultures which not only grew well within the capsules when in the peritoneum of these birds, but had acquired the power of killing them when inoculated in the usual way. Although the guinea-pig resists infection with avian bacilli, Dr. Baldwin has noted at the Saranac Laboratory that this variety of the tubercle bacillus if passed through several rabbits, which it kills by intravenous injection in about twenty-five to thirty days, has become so altered that it has acquired virulence for the guinea-pig, and will then kill these little animals as well as the human bacillus does.

Pathology.

Among the problems in pathology which require to be studied are:

(a.) The chemical changes in the quality of the digestive secretions, ptyalin, pepsin and trypsin, which in common with the infectious diseases occur in tuberculosis, and their immediate causes.

(b.) Further studies of the blood in tuberculosis. The cause of the anæmia in this disease; whether due to the effect of the toxins directly on the blood cells or the blood forming tissues, or indirectly on the nerve centers, and the nature of this process.

(c.) We also need light on the exact pathological changes which result in cure in peritoneal tuberculosis after laparotomy, and the mechanism by which tubercle bacilli (usually so resistant to the action of the tissues) are disposed of in the cure which follows this operative procedure. Does tubercle represent a defensive effort on the part of the organism, or is it a nidus which favors the multiplication and subsequent dissemination of the germs? What are the causes which lead occasionally to the entire disappearance of the bacilli before death in acute miliary tuberculosis from the tuberculous lesions of man and animals, and what evidence is there that we may interpret this disappearance as indicative of an acquired immunity?

(d.) What are the factors determining local immunity in the tuberculous? Is it true, as Koch pointed out, that the tuberculous individual is relatively immune to reinoculation with the virus (just as the syphilitic cannot be reinfected during the active progress of the disease)? How are we to harmonize this view with (i) local extension of the disease; (ii) extension of disease in other regions, *i. e.* development of laryngeal secondary to pulmonary tuberculosis?

(e.) Very divergent opinions are held by capable observers with regard to the meaning of the presence of tubercle bacilli in milk, semen, urine, etc. The majority are of the opinion that wherever they are present in the excretions there must be active tuberculosis in the excreting organs. On the other hand, a large number of cases are on record in which no such tuberculosis has been discovered; and the conclusion reached is that the actual excretion of bacilli by the kidneys, mammary glands, testes, etc., may occur. The question ought to be settled, *i. e.* by intravenous inoculations and observations upon the secretions at successive periods to determine (i) the earliest period at which the bacilli are discoverable in the secretions; (ii) the possible taking up of bacilli by endothelial and gland cells in the excretory glands; (iii) the difference, if any, in the appearance and properties of bacilli cast off by ulceration into the secretions and those truly excreted.

(f.) The production both within the body and outside of "beading" of the tubercle bacilli; its meaning; whether such beaded forms are degenerate or resistant forms (due to reaction of bacilli towards body fluids); relationship, if any, between beading and spore formation; what is the true nature of the tubercle bacillus? Is it a bacillus at all?

Prophylaxis.

We need still further studies on the various sources of infection. Until recently we have looked upon the dried sputum of pulmonary tuberculosis, the dejections from the bowels of patients suffering from tuberculous enteritis, and the milk of tuberculous cows, as practically the only sources of infection to be guarded against. That the dried sputum is not the only source of danger has been shown by the recent work of Flügge,[2] who has demonstrated that the throat and mouth secretions of most tuberculous patients when atomized by the act of coughing may be a real source of infection to those about them. Some method of determining to what extent this source of danger exists, and which types of cases are most apt to thus spray bacilli about them in fine particles of saliva or throat mucous, would be of great value to preventive medicine.

Dr. Baldwin's[3] studies at the Saranac Laboratory have also shown that the hands of patients using handkerchiefs may, in the majority of cases, be the carriers of unsuspected bacilli.

Practical suggestions as to the education of the masses in regard to the sources of infection, and studies which will give us more light on the best and most practical methods to guard against them, would be of inestimable value. Under this head would be comprised practical suggestions as to the care of dust in living rooms, cars and public buildings, and better methods of the disinfection of these places by artificial means; as well as improved plans for ventilation and light in buildings, and the general dissemination among the masses of a better knowledge of personal hygiene.

A most promising prophylactic measure would be the establishment of state and municipal sanitaria in favorable localities for the treatment of incipient cases, and of special hospitals on the outskirts of large cities for the care of advanced and hopeless ones. It does not seem unreasonable to hope that a general adoption of this plan would in itself materially reduce the mortality from tuberculosis directly by curing a fair proportion of cases, and by the educating patients as to the care of their health, and indirectly by removing from crowded communities a large number of individuals who are a constant source of danger to those about them. More facts bearing on sanitaria, their location, construction, equipment and administration, would be of inestimable value.

The production of relative immunity by preventive inoculation belongs to the field of prophylaxis, and offers a most enticing subject of study; but I will refer to this more fully later on.

Bacteriology.

Studies relating to artificial methods of exalting and attenuating the virulence of the tubercle bacillus are much needed, as they bear directly on the possibility of producing artificial immunity by preventive inoculation, and of obtaining an efficient antitoxic serum for the treatment of the active forms of the disease. Other bacilli, like the smegma bacillus and the bacillus of timothy-grass, which present nearly the same morphological appearances, the same peculiar reactions to staining methods as the tubercle bacillus; the bacteria which produce pseudo-tuberculosis, offer a most interesting field for further research.

Further light on tuberculin, the best methods of obtaining this toxin of standard strength, the influence of the virulence of the germs from which it is produced, and of the culture medium on which they grow, the technique of manufacture, etc., would be of great value. Dönitz[4] has recently shown that specimens of tuberculin obtained from different sources vary in strength as one in three.* In relation to this subject my own observations so far have tended to the belief that as efficient a tuberculin can be made from attenuated as from virulent cultures, but as the non-virulent cultures grow generally more luxuriantly it may be that they produce more toxin, though of less potency, while the virulent germs elaborate a more toxic product but less in quantity.

It is greatly to be desired that physiological chemistry shall separate the various substances elaborated by the bacilli or contained in their bodies, and that the toxicity of each of these shall be determined and their influence on the cell and the living animal studied. Researches in this direction have been begun by Drs. Levene and Baldwin at the Saranac Laboratory. Dr. Levene[5] has already found that "the body substance of tubercle bacilli does not contain any products of the albumin nature; that like the nuclei of cells it consists mostly of nucleoprotcids; that one of the nucleoproteids differs from all the other nucleoproteids inasmuch as it is not precipitated by magnesium sulphate (and in this point resembles nucleohiston), and does not give the Biuret test; that it contains nuclein or nucleins as such." The three different proteid substances contained in the bodies of the tubercle bacillus have different coagulation points; the first from 50 to 64°C., the second from 72 to 75°C., the third from 94 to 95°C., the last being very rich in phosphorus. Dr. E. R. Baldwin is about to make some experiments bearing on the toxicology of these three proteids. As such large quantities of dried T. B.'s are necessary for each chemical and toxicological experiment the completion of the work necessarily will require some time. Researches on the chemistry of the tubercle bacillus have also been published recently by Ruppell,[6] working in Behring's laboratory, and by Jules Auclair,[7] from the laboratory of Professor Grancher.

A most promising field of research has recently been opened by the successful cultivation by Nocard of various microorganisms enclosed in celloidin capsules and inserted into the peritoneal cavities of living animals. These little celloidin cells allow to a limited extent the passage of some of the animal fluids into the capsule, thus affording a sufficient pabulum for the growth of the germ while protecting the microbes from the direct action of the body cells, and also permit the toxic substances elaborated by the bacteria to pass through and be taken up into the general circulation, while egress of the germs and their dissemination throughout the system of the animals is prevented. Experiments by these methods offer two very broad fields: the study of the influence of cultivation under such conditions upon the germs, their virulence and their products, and the study of the effect of freshly and continuously elaborated toxins on the living organism while the latter is protected from the direct pathogenic consequences of the spread of the microbe throughout the system at large. We may hope by this line of research to obtain more light on the mechanism of infectious diseases, and the reactions of the living tissues to the toxic products of the microbes, and it would seem to open new possibilities in attempts at the successful production of artificial immunity and the obtaining of antitoxic substances for the treatment of diseased conditions.

After prolonged cultivation by this method Vincent[8] succeeded in changing the harmless varieties of saprophytes into parasites, which gradually acquired the power of producing toxins, and ultimately of killing animals. Nocard[1] found, as

*As in the use of tuberculin for diagnosis the test is only a qualitative one, the practical importance of such variations is somewhat lessened.

already mentioned, that the human tubercle bacillus, which is non-pathogenic for fowls, after cultivation within these celloidin capsules which had been inserted into the peritoneal cavity of chickens, acquired after a time the power to kill these animals when inoculated in the peritoneum.

We need further knowledge on the relative pathogenic properties for man of the recognized varieties of the tubercle bacillus, the human, the bovine, and the avian.

Diagnosis.

The value of any addition to our knowledge which will enable us to make a positive diagnosis at the earliest possible moment after infection has occurred must be conceded, for the chance of cure depends greatly on the early detection of the disease, and observations in the autopsy room have taught us how often nature can cure tuberculosis in its incipiency. We should in many cases no longer be content to wait for the appearance of expectoration containing bacilli, for marked physical signs, or for an unmistakable clinical picture. It seems to me we have in the tuberculin test a most delicate and searching means of detecting tuberculous disease when this cannot be done positively in any other way. We need more exact knowledge concerning the practical application of the tuberculin test in man, and we greatly need more light on the best method of applying this test, its exact value, its errors, their cause, and its possible dangers; in what other pathological conditions the reaction to tuberculin may occur; —and are the reactions which take place with considerable frequency in other diseased conditions due to them, or do they invariably indicate a concomitant and unsuspected tuberculous focus in some part of the body?

We need to know more as to the mechanism of the tuberculin reaction. The most generally accepted theory at present in regard to it is, briefly, that the small dose of tuberculin injected is a partly specific irritant both to tuberculous foci and to the susceptible organism in general. It produces intense hyperæmia of all tuberculous tissue in the body (local reaction), and as the result of this hyperæmia much toxin stored up in the tubercles themselves is thrown into the general circulation and produces fever and the characteristic symptoms which go to make up what is termed "a general reaction." That these poisons stored up in the tubercles are in part at least derived from the dead or weakened bacilli has been shown by the experiments of Babes and Proca,[9] who found that if two sets of rabbits be injected with equal quantities of living and dead bacilli the latter react to the tuberculin test at a much earlier period than those inoculated with living germs. This hypothesis that the general reaction is brought about by the toxins already stored up in the tuberculous lesions and exploded as it were by the hyperæmia produced about these lesions as a result of the test injection of tuberculin, is borne out by the fact that a greater amount of albumose can be recovered from the evaporated urine collected during the reaction than was contained in the test injection; also by clinical observations which indicate that patients suffering from localized surgical tuberculous processes of limited extent, and where the vascular supply to the part is limited, require a larger test injection to produce the reaction than those who have extensive or scattered visceral lesions in highly vascular organs like the lungs.

A very general impression seems to prevail that the tuberculin test is dangerous and tends to aggravate the disease. This impression had its origin, no doubt, in Virchow's statement that the autopsies which he made upon the first patients treated after Koch's method by repeated and increasing doses of tuberculin, so as to produce frequent and violent reactions, revealed in an unusual number of instances the presence of apparently new tuberculous foci at a distance from the original and recognized lesions. It may be conceded that violent and repeated reactions when brought about in patients suffering from extensive visceral disease tend to exhaust the already overtaxed defensive resources of the organism, and may in this way aggravate the disease. But the conditions are very different in incipient cases where the resistance of the patient is as yet but little impaired, and where it is necessary to produce only one moderate reaction. Even if the correctness of Virchow's observations be conceded, the finding of more pronounced and distant lesions may not necessarily mean that the bacilli were disseminated through the system as a result of the tuberculin treatment. We have ample clinical and experimental evidence that the local reaction resulting from an injection of tuberculin makes apparent the presence of latent and unsuspected tuberculous lesions, but no proof has been brought forward to show that the bacilli are scattered through the system or that new foci are produced as a result of such injections.

In a recent study by A. Broden[10] on the Treatment of Experimental Tuberculosis of the Peritoneum in Dogs by Tuberculin Injections, he points out that the extent and number of tubercles visible in the peritoneum when the treated animals are killed at an early stage of the disease are greatly in excess of that noted at the same stage in the controls. On careful microscopical study, however, these large and more numerous tubercles are found to consist of an aggregation of leucocytes, which appear to represent a defensive effort on the part of the system to limit the disease, as the bacilli in them are seen to be very few in number, beaded, and soon entirely disappear, leaving only slight fibrous lesions from which the animal ultimately completely recovers. In the controls killed at the same period the macroscopical appearances show but little evidence of disease, but a microscopical study of the peritoneum reveals everywhere small nodules swarming with large numbers of short, well-stained bacilli, the disease going on rapidly to a fatal termination.

In my experience no injury to the patient has occurred thus far as a result of a test injection of tuberculin where small graded doses at two or three intervals have been used for diagnostic purposes, and all of the hospital physicians with whom I have conversed, who have practiced this method, have apparently had a similar experience, and none, to my knowledge, has abandoned it on account of any evidence of injury to the patient. If we consider the overwhelming importance of this subject in our struggle against tuberculosis, it is greatly to be hoped that a thorough study of the method will bring to light the true facts as to its exact value, and its limitations and possible objections.

The application of X-rays to the diagnosis of incipient pulmonary tuberculosis promises to be of practical assistance, as the height of the excursion of the diaphragm and the appearance of a slight shadow over the suspected area in the lung, when considered together with the rational symptoms and any trifling deviation from the normal sounds in the lung, enable the physician to reach a positive conclusion in many cases before the appearance of expectoration containing bacilli, or the unmistakable symptoms of the disease are present. A case I saw recently with Dr. Francis Williams, of Boston, illustrates the corroborative value of an X-ray examination in early and doubtful cases, and that by a combination of the usual clinical methods with a thorough X-ray examination, a positive conclusion as to the presence or absence of the disease may often be reached before cough and expectoration are present, or any appreciable deterioration of the general health has occurred. I had suspected the presence of tuberculosis in a hospital patient of Dr. Williams' merely because the temperature chart showed a rise of one-half to one degree occasionally in the evening, and because I thought I could detect very slight evidence of consolidation at one apex. These were all the symptoms present. Under the X-ray the case showed that the diaphragm on the suspected side was higher than the normal, and its excursion appreciably diminished on that side, while a slight shadow could be made out at the apex. I suggested the tuberculin test, and the patient had a typical reaction, the temperature reaching 102.5, fourteen hours after the injection.

Treatment.

The climatic and open-air treatment of tuberculosis in especially constructed sanitaria is at present conceded to offer the patient the best chance of recovery, but this needs elaboration, and studies which would afford more exact indications for such class of cases as to the proper application of rest or exercise, exposure to the air, feeding, hydrotherapy; the use of tonics and reconstructives, and the regulation of the smallest details of the daily life, would be of great value.

The obtaining of a serum that would be antitoxic for the infections concurrent with tuberculosis would make us much less hopeless in the presence of such cases, while at present we must be contented to rely on fresh air, rest, food and alcohol to relieve this desperate condition.

To laboratory researches we may yet look for some general specific method of treatment, either by preventive inoculation or the production of an efficient antitoxic serum for tuberculosis. It is true that, in spite of the claims so constantly made, little of practical value to the tuberculous patient has been accomplished so far by the enormous amount of research work bearing on attempts to produce immunity in animals against tuberculosis and to obtain an efficient antitoxic serum for the poison of this disease.

To many minds there seems no reason to hope that any efforts tending to the production of artificial immunity in this disease will ever be successful, and it is true that little can be found in the clinical history of tuberculosis which would lead us to believe that such an immunity ever occurs in the natural course of the disease, as recovery from a tuberculous manifestation in any part of the body does not seem to afford any protection against a subsequent and often fatal outbreak of the malady. It would be presumptuous, however, in view of the recent advances made in this direction in other infectious diseases, to deny absolutely the possibility of solving this problem, and some experimental evidence is accumulating of late which tends to prove that the resistance of the body to a virulent tuberculous infection can be greatly increased by preventive inoculation.

I will not here review the work done in this direction by Richet, Héricourt, Grancher, Martin and others, as it is no doubt familiar to you, but I will occupy your time by referring, more particularly to my own experience in this direction, not on account of the practical value of the results I have obtained, but because my observations having been made entirely independently seem to add some confirmatory evidence to the partial success already attained by others in this field. In common with many other experimenters, I failed to obtain any appreciable results by preventive inoculations of the various products to be found in liquid cultures or by the inoculation of the bodies of dead tubercle bacilli. I was driven, therefore, to attempt to reach the end in view by making use of the living germs themselves, attenuated by various methods.

The first evidence of any protection which I succeeded in obtaining was in 1893, which I detailed in a paper read before the Association of American Physicians in May, 1894. I found that by subcutaneous preventive inoculations of attenuated living cultures of avian tubercle bacilli I was able to increase the resistance of the rabbit to infection with virulent living mammalian culture. The photographs which I show you demonstrate the degree of immunity obtained. The test inoculations were made in the eye, where the immediate result could best be studied and controlled. The eyes of the controls were gradually destroyed by the progressive tuberculous process, while those of the vaccinated animals, after undergoing a certain inflammatory reaction, returned more or less completely to their normal condition. Unfortunately, many of the animals died of the attempt at vaccination, and complete immunity was manifested only in a few; while in others, similarly treated, the eyes were eventually either partially or totally destroyed. I have also obtained a marked degree of success in protecting guinea-pigs by cultures of mammalian bacilli attenuated simply by prolonged growth on artificial media.

Dr. de Schweinitz[11] was the first to call attention to his results in protecting guinea-pigs by means of living attenuated cultures, and although my results have not thus far been as good as his, my experience in the past four years shows that a very marked degree of increased resistance to tuberculous infection can be induced in these animals, as well as in rabbits, by such preventive inoculation. It is of interest to note that the culture used by Dr. de Schweinitz in his experiments was originally obtained by him from me, and is the same with which my own experiments were made. This culture originated from plants made on serum by me from the lesions of a rabbit infected with human tuberculosis in 1891, and has been grown on various media, principally on the ordinary

glycerin peptone bouillon, either neutral or slightly acid, ever since. I began to notice, after two years' cultivation, that a great majority of the guinea-pigs inoculated with this culture lived for many months beyond the usual time, and the virulence of the germ was evidently decreasing. It was not, however, until 1894 that I observed that many of these animals apparently recovered completely from the inoculation, while a few still died of chronic tuberculous lesions. At present, if twenty animals be inoculated with this attenuated germ, which has been grown for six years continuously on artificial media, with perhaps one or two exceptions, all survive for many months. It has been necessary, however, to keep the pigs for a long time, for occasionally some of them die of chronic tuberculosis even two and a half years after the attenuated inoculation.

What the attenuation of the bacillus is due to is still a matter of doubt in my mind. De Schweinitz is of the opinion that the acid in the media greatly hastens the attenuation, and has therefore grown his cultures on very acid media; but the germ undoubtedly loses its virulence if the cultivation is sufficiently prolonged, no matter what the media may be. I have varied the acidity of the media, but as yet have come to no definite conclusion on this point. In favor of Dr. de Schweinitz's view it may be stated that the tubercle bacillus loses its virulence much more rapidly while growing on potato which is slightly acid, than on serum, but these two media differ also in many other respects besides in reaction.

It is a well-known fact that any living organism loses any attribute which through many generations its environment does not call into use. While living a saprophytic existence the tubercle bacillus has no need for the exercise of that characteristic which is known as its "virulence" and which means the power to cope successfully with the resisting elements of living tissues, and it may be that this attribute is lost to it by its disuse through the millions of generations the germ passes through while growing for so long on artificial media. However that may be, it is certain that the tubercle bacillus is robbed of its virulence with the utmost difficulty. All other methods of attenuation hitherto employed—heat, time, antiseptics, etc.—aim a blow at the viability of the germs sought to be attenuated, but do not alter their biological characteristics. They are either killed, in which case they produce no disease, or else they survive sufficiently to grow in the body and ultimately destroy the life of the animal. Prolonged cultivation, on the other hand, gives us a culture which grows vigorously, but which has lost to a great extent its specific pathogenic powers.

A certain disturbance of health and loss of weight are always caused by the inoculation of this attenuated culture, but the animals after three months seem to have completely recovered. If at this time they are inoculated with virulent bacilli, together with an equal number of controls, the prolongation of life in the vaccinated animals will be apparent in every case. In several lots I have noticed the death of all the controls to occur before a single vaccinated animal had died. Complete immunity, however, has not been attained in my experience so far by this method, although some of the animals have occasionally lived as long as eighteen months after the virulent inoculation.

I will not weary you with any of the details of these experiments, which are still incomplete, but merely report the gross results which I have obtained thus far in work done on a total of one hundred and twenty-two guinea-pigs. In 36 controls the average life was 57.2 days, and in the 66 vaccinated animals it was 154.3 days, so that the vaccinated animals lived nearly three times as long as the controls. Some of the pigs survived the virulent inoculation as long as eighteen months. This includes all the experiments on guinea-pigs, some of which were made before the germ was very much attenuated. Intravenous inoculation of this attenuated culture protects rabbits to about the same extent, but in them, as in the guinea-pigs, the immunity is relative except in a few cases where the protection seems to be almost complete.

It would seem at first sight that the evidence brought forth by these experiments tends to prove positively that at least relative artificial immunity had been produced in these animals. The evidence is incomplete, however, in so far as it relates to the complete recovery of the animals from the protective inoculation. I have kept vaccinated pigs which lived nearly three years in apparently good condition and yet ultimately died of chronic tuberculosis. It is possible, therefore, that these experiments only prove that the disease is not auto-inoculable, and that an animal in which a very chronic form of tuberculosis has been induced artificially is not susceptible to reinoculation with a more virulent infecting material. This, I believe, is true of syphilis, a disease which closely resembles tuberculosis in its course and various manifestations.

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INFUSION OF SALT SOLUTION COMBINED WITH A SPECIAL METHOD FOR THE ADMINISTRATION OF OXYGEN INHALATIONS AS A TREATMENT IN PNEUMONIA.*

By Clement A. Penrose, M. D.

It has been the custom in the Johns Hopkins Hospital for several years to use infusions of normal salt solution (.6%) in cases of collapse, especially during or after severe surgical operations. In such cases the pulse is generally the index to the necessity for infusion or the amount infused.

During my gynæcological service in this Hospital I had the opportunity of observing the effects of infusions in a number of such cases, and was much impressed by the fact that in many the stimulation to the respiration was more marked than to the heart. This was true especially of those cases who, taking the anæsthetic badly, were in a more or less state of asphyxia.

The possibility of this respiratory effect being in addition to others of great benefit in conditions like pneumonia occurred to me then, but it was not until I had entered the service of Dr. Osler that the opportunity arose to demonstrate the truth of such speculations. He kindly permitted me, February 14, 1898, to try the effect of salt infusions as a last extremity in a very grave case of pneumonia, to whom later inhalations of oxygen were administered after a special manner. Since then the same treatment was used by me in two other cases of pneumonia; one, on the surgical side following an operation, and the other in private practice.

The infusions of salt solution were given in the usual fashion employed in the Hospital, *i. e.* the salt solution, at a little above body temperature, is poured into a graduated bottle, from the bottom of which runs a long rubber tube. The needles, which are introduced under the breast, or into the subcutaneous tissues of the thighs, etc., are connected with this tube. The pressure is regulated by elevating the bottle or by means of a rubber bulb, with valves, which is attached to the stopper of the bottle, and thus air can be forced into the space above the salt solution. At intervals a careful examination of the heart is made, especial attention being paid to the second pulmonic sound, with instruments in readiness for instant bleeding if this become too accentuated or murmurish in quality. Inhalations of oxygen in connection with infusion are given according to a special method, which is as follows:—in place of the delivery nozzle usually adopted, a glass funnel is substituted, which is held by a framework resting on the bed about two inches from the face, and supplies oxygen to both mouth and nostrils without interfering in any way with the breathing. The oxygen is passed through a wash bottle containing a pint of hot water in which has been placed one dram of an inhalation mixture, the formula of which is:—

℞

Creosoti (beechwood), . .	℥ ss (one-half ounce.)
Olei Terebinthinæ, . . .	℥ ss (one-half ounce.)
Tr. Benzoini Comp. . . .	℥ ii (two ounces.)

The inhalations are given at intervals whenever lips or finger tips become bluish, are continued till the color is normal, usually from ten to fifteen minutes in those who give a good reaction.

The first two cases of pneumonia on which I have tried infusions of salt solution combined with this special method of giving oxygen inhalations died, the last case made a perfect recovery. It should be remembered, however, that all these cases were considered hopeless, and had received the usual treatment for pneumonia before this method was resorted to. Since I left the Hospital, September 15, 1898, this treatment has been resorted to in several other severe cases, and also by physicians in the city in their practice, with most gratifying success. In the two cases that died, the prolongation of life and the relief of symptoms, etc., were so marked that I regretted this treatment had not been employed earlier. From the brief histories which are presented, it will be seen that all three cases represented the severest types of pneumonia with every reason for unfavorable prognoses.

Case I, J. O., admitted to Ward F (medical) February 12, 1898, on the 5th day of the disease. The patient was an ill-nourished, feeble man of fifty-two years, with a bad alcoholic history, complete consolidation of the right lung, a temperature ranging from 104° to 105.5°, and a muttering delirium, with twitching of the muscles, who in addition had chronic Bright's disease, with almost anuria for two days after admission. The pulse was very weak and wavering, 104 per minute, respiration shallow, labored and ranged about 40 per minute. Dr. Osler saw the patient two days after admission, the day upon which infusions were begun, and said the man was moribund, and would probably not live till night. The results of infusion were most surprising. On the first day, after 2700 cc. salt solution had been infused, the following was noted:—"the pulse became full and regular; the rate however remained about 104, respirations became deeper and fell to 28 per minute." On the second day 4000 cc. more of salt solution were infused. The patient became conscious after three days of muttering delirium, and voided large quantities of urine. The pulse and respirations remained about the same. On the third day 3000 cc. salt solution were used with little effect. The pulse was 112, and respirations 44 per minute.

On the fourth day of treatment 3000 cc. of salt solution were infused. The temperature fell to 100.4°, and the patient had a profuse perspiration. A crisis seemed imminent. Later however the pulse ran up to 140, and respirations to 52, and as considerable cyanosis developed, inhalations of oxygen were given according to the special method mentioned above. Almost immediately the patient's lips and nails became a brilliant red. He went to sleep, and the tongue and mouth were noted to be much less foul. The pulse remained about the same, but respirations fell from 56 to 52 per minute, and

* Read before the Medical Society of the Johns Hopkins Hospital, Monday, January 23, 1899.

became less labored. Oxygen was afterwards given at intervals with great comfort to the patient, the inhalation mixtures seeming to have an expectorant action, as the sputum became less tenacious and more watery, due, no doubt, in part to the salt infusion.

On the fifth day (twelfth day of the disease), patient began to fail and required 6000 cc. of salt solution throughout the day, with almost a constant supply of oxygen. The pulse was 140 and very irregular; respirations were 56, and shallow. About noon I bled the patient from the arm and removed thirteen ounces of a dark, quickly clotting blood. This was done because the second pulmonic heart sound became distinctly murmurish. The pulse fell after the bleeding from 140 to 132, respirations from 56 to 32, and again, a good reaction to oxygen was given. The patient lived all day in a semi-conscious condition, but at 9.30 P. M., died very quietly in spite of all further efforts.

The leucocytes in this case fell from 16,000 the day infusions were begun, to 9200 the day of death.

Case II, Dr. B., admitted June 26, 1898, Ward C (surgical side). The patient was a large, stout man aged fifty-two years; good family history; operated on July 11, for carcinoma of the tongue; right half of tongue removed, with glands of neck, etc. The anæsthetic used was chloroform. Pneumonia followed the operation on the sixth day, due to aspiration of food. It was patchy in character, and scattered throughout both lungs.

On the second day after the development of pneumonia, the patient's condition became so desperate that salt infusion combined with inhalation of oxygen was begun. In this case the same good effects were noted as in the former. In addition, the wound in the neck which, with the half of tongue remaining, had become very foul and offensive, in a few hours became quite clean and sweet. The patient died on the fourth day of the pneumonia, having received 13,000 cc. of salt solution in all. He showed, though in a very low condition, marked reaction to oxygen after being infused.

Up to this time little had been accomplished as far as mortality was concerned, but in one case, I was contending with age and alcoholic history, and Bright's disease, and in the other with an aspiration pneumonia following a severe surgical operation; in both cases the treatment was employed late in the condition and as a last extremity. Recently I have had a case in private practice where the conditions with the exception of age seemed even more hopeless than in the other two, but which has made a remarkable recovery and fully compensates for the disappointment of losing the other two patients after they had shown such evident improvement.

Case III, Mrs. R., aged 34, married. Delicate constitution; had a slight cold for two to three days, in all probability, an attack of grippe, which was then epidemic. December 16, 1898, while standing before an open window, she felt a stabbing pain in the left side, which increased in severity. She went to bed and sent for the family physician. Her temperature rose steadily, and on December 19, four days later, reached 104°. The patient then became delirious and had, according to her physician, decided flatness throughout the upper left chest. The pulse was weak and thready; respirations rapid and shallow. The delirium in spite of treatment persisted, and the patient became progressively weaker. I was called in, in consultation, upon December 26, at 10 A. M. Her temperature was then 105.5°, her pulse irregular, 120 and over, very soft and weak, running in character. Respirations varying from 48 to 52 per minute were very shallow and labored; lips and finger tips much cyanosed. The patient was in muttering delirium, with marked twitching of the muscles, especially those of the extremities. The muscles of the neck were somewhat stiff. Her condition was so desperate that a thorough examination was out of the question. However, numerous crackling râles were heard throughout both chests and in the left upper front, the breath sounds had a decidedly tubular character. The back was not examined. 1000 cc. of normal salt solution were immediately infused in the right breast, and inhalations of oxygen were begun by my method, with immediate benefit. Respirations fell to 32 per minute and the twitching of the limbs grew less and the patient regained a normal color in a few minutes. The pulse showed some improvement in volume and tension, but the rate remained still about 120. Inhalations and repeated cold sponges were given all day at intervals, but with little improvement. The temperature fell a degree or so, but the meningeal symptoms became much more marked. At eleven P. M. severe convulsions set in, almost eclampsic in nature, and succeeding one another every three to four minutes. The patient was very blue. 2000 cc. more of salt solution were infused, and eight ounces of blood were removed from the left arm as the second pulmonic sounds had become murmurish. The blood was very dark and clotted immediately on standing. There was now decided improvement; the respirations fell from 48 to 24 per minute (just one half), and the oxygen which had apparently been of little service all day, in a short time gave a good reaction. The lips and nails became a good color; respirations steadily grew deeper and less labored. The tongue and mouth became cleaner and more moist, the pulse steadier and fell to 104 per minute. The convulsions gradually disappeared.

December 27, 4.30 P. M. The patient is much better, is conscious after *eight days* of muttering delirium. The temperature is 105.5°. She takes nutrition well, has voided much urine, and perspired freely. 600 cc. more salt solution were infused, and the rectum was irrigated with large quantities of this solution also. Oxygen was given at intervals to the patient more for her comfort than because of cyanosis. Mouth and tongue continued moist and clean; the breath was sweet, with a strong odor of the inhalation mixture.

December 28. Temperature 102°; general condition much better; pulse is full and strong, regular and 117 per minute; respiration only 30, quiet; oxygen is now discontinued. From this time on the patient steadily improved; the temperature fell gradually by lysis, and on January 14, was normal. She has now fully recovered, has gone to the country, and has already gained several pounds. I consider this a remarkable case, a veritable resurrection, and which fully repays one for the time spent in vain on others. With such a high temperature, with muttering delirium for eight days and later convulsions, with grippe as a precursor to the pneumonia, in a naturally delicate woman, I am sure all will agree that the

prognosis was more than bad. The blood in this case was negative for the Widal typhoid test, the urine showed a considerable number of pus cells from a leucorrhœa, but no casts, etc.

In conclusion, I claim that the infusion of salt solution in pneumonia is a decided advance in its treatment if used by those familiar with the significance of the second pulmonic heart sound, and who are prepared to bleed immediately if this indicates danger. In my opinion, infusion, which is slower, is preferable to transfusion. It dilutes the toxines in the blood, relieving delirium, etc., and promotes their elimination through the sweat glands and kidneys. It lowers the temperature. It stimulates the heart. It lowers the rate of respirations and renders the breathing less labored. It seems undoubtedly to *render the patient more susceptible* to the influence of oxygen.

The use of a funnel in the administration of oxygen held by a framework has these advantages:

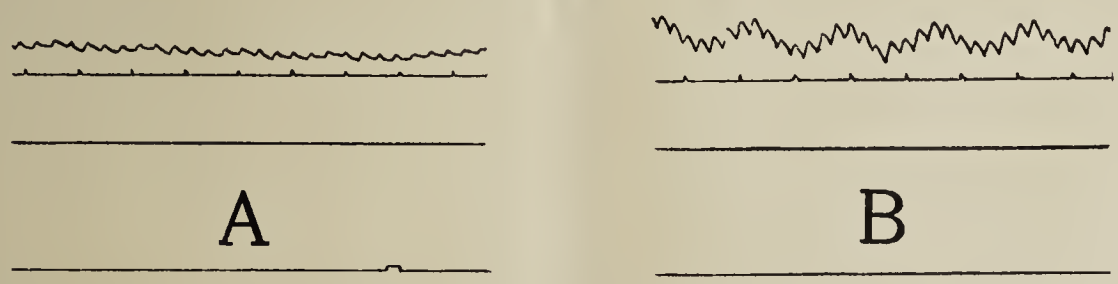
The patient gets oxygen through both the nostrils and mouth. There is no impediment to expiration, as is the case with a nozzle in the nose or mouth. The patient may go to sleep and still take the oxygen, which they frequently do, whereas the nozzle being uncomfortable and producing a blast, is apt to keep them awake. The passage of the oxygen through a hot inhalation mixture is more beneficial than when used alone. The vapors from such a mixture carried over with the oxygen certainly render the tongue and mouth less foul, the breath sweet, and promote expectoration,—and who can say it does not have some antiseptic effect on the lungs?

Oxygen alone being odorless, a patient if conscious will make greater efforts to breathe something which is tangible, and will not turn the head away, etc.

That cases which have been previously infused with salt solution react much better to oxygen has certainly been my experience. I have tried oxygen alone in several cases of pneumonia, and have the notes of the same with me, but not one, although representing pneumonias of a much less severe type, gave the remarkably quick reaction noted in the three cases where infusions of salt solution had been previously given. Oxygen, it is known, is held in the blood in two ways:—as a chemical compound with hæmoglobin and in solution; increasing the bulk of blood may increase its oxygen-carrying capacity as a whole, although diminishing it relatively; hence the advantage of supplying more oxygen.

Dr. Reid Hunt, of the Johns Hopkins University, has kindly told me of some experiments which he has made in the Biological Department on the effect of intravenous injections of saline solution into dogs. He finds that in curarized dogs in which artificial respiration is maintained, the injection of normal saline solution, or of Ringer's solution, will cause a marked increase in the amplitude of the respiratory undulations of the blood pressure. This change often occurs before there is any rise of blood pressure or appreciable change in the pulse rate. He thinks it is due to a larger volume of blood passing through the pulmonary vessels. The accompanying kymograph curves are taken from one of his experiments. A is a portion of the record before; B, after the injection of 700 cc. of warm Ringer's solution into the saphenous vein of a curarized dog.

In this, we would have then an experimental proof of my clinical observation, viz., that infusion of salt solution increases the circulation in the lungs, and therefore their ability to take up more oxygen. The oxygen capacity being increased as a whole by increasing the bulk of blood, gives us an additional factor.



A NOTE ON THE PIGMENT PRODUCTION OF BACILLUS PYOCYANEUS AND BACILLUS FLUORESCENS LIQUEFACIENS.

By Paul Gerhardt Woolley, B. S.

(*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*)

Some time ago while studying cultures of B. pyocyaneus and B. fluorescens liquefaciens, the similarity of the pigments produced by these two organisms seemed to me to indicate a possibility of interchangeability of chromogenic function. In these two particular cases the chromogenic peculiarities on agar-agar of the B. pyocyaneus seemed to be more nearly like those of B. fluorescens, while chloroform solutions of the pigment from agar-agar cultures of B. fluorescens showed a faint trace of blue.

Babes, Fordos, Gessard and Kuntz showed long ago that B. pyocyaneus produced three pigments, one fluorescent, not soluble in chloroform, one blue, soluble in chloroform, and the other a red, pyoxanthin, supposed by Gessard to be an oxide of pyocyamin or the blue pigment.

Since these observations Gessard, Wasserzug and others have shown how easily achromatic and monochromatic varieties or "races" could be produced artificially.

What I intended to do was to place B. fluorescens lique-

faciens, which is the fluorescent bacillus most nearly akin to B. pyocyaneus in cultural and microscopic characteristics, under conditions most favorable for production of pyocyanin and see whether or not a "race" could be obtained which would produce pyocyamin. For this purpose I used the medium known as *Gessard's Agar*, which is a neutral mixture of agar-agar, peptone and glycerine, and which Gessard found to be the best medium for forcing B. pyocyaneus to a maximum production of its blue pigment with a minimum of the other two pigments. In these experiments I used samples of B. pyocyaneus obtained from six different sources, and samples of B. fluorescens from five sources. These were grown at room and blood temperature. Each culture made was allowed to grow for three days and then cultures were made on fresh media from the cultures already grown. In this way an uninterrupted series of cultures was made from each specimen of the organisms, and extending over twelve transplantations.

The result however was negative. For one or two generations two of the fluorescent varieties did give some blue pigment soluble in chloroform, but at the end of the series all of the cultures of B. fluorescens were colorless, and only one of the cultures of B. pyocyaneus was typical. That one was a specimen for which I thank Dr. Jordan, of the University of Chicago. Evidently the color-line is not to be crossed.

Besides these results, I was able to confirm the statements made by Gessard, Noesske and others that the absence of phosphoric acid in some form inhibits the production of fluorescence. I also am able to state that the magnesium in Uschinsky's fluid can be replaced by aluminum with no effect upon pigment production.

EXPERIMENTS MADE TO DETERMINE THE EFFECTS OF SUGAR UPON THE PIGMENT FORMATION OF SOME OF THE CHROMOGENIC BACTERIA.

By Paul Gerhardt Woolley, B. S.

(*From the Pathological Laboratory of The Johns Hopkins University and Hospital.*)

Uniformity in the composition of culture media is one of the requisites of uniformity of observation in the study of bacteria in cultures. This is evident on its face; and yet it is probable that in the study of the bacteria in laboratory media the fact that a certain amount of sugar is present is not sufficiently considered, in spite of the fact that, in some conditions, for instance in the production of toxins by the B. diphtheriæ, the presence of sugar makes a great deal of difference. Of course the quantity of sugar in the ordinary bouillon media is very small, but it is large enough to allow B. coli communis some exercise of its fermenting functions, and is therefore appreciable, and may also make appreciable differences in results in observations. It was in view of such facts as these that I set out at Dr. Flexner's suggestion to make a series of experiments with sugar-free and sugar-containing media to see what the effects of sugar upon certain functions of certain bacteria might be.

For these experiments the chromogenic bacteria seemed to be best suited, one reason being that many of them are known to be prevented from producing their pigment in the presence of sugar, and this, if true, would make it easy to determine with greater or less certainty the relation between the chromogenic powers of the organisms and the sugar present in the medium.

As examples of the chromogens, I selected B. pyocyaneus, B. fluorescens liquefaciens, B. janthinus and B. prodigiosus. As examples of the sugars I used glucose, lactose and saccharose.

In order to have a sugar-free medium as a means of making "check" observations, I treated bouillon made from fresh beef, by the method of Theobald Smith, the essential of which is the destruction of the sugar, present in such an extract, by the help of B. coli communis. To this bouillon when rendered neutral and prepared in the usual way were added definite quantities of the three sugars. For the purposes of the experiments I used a 1 per cent. and a 2 per cent. solution of each of the three sugars. In all the experiments cultures were made in the sugar-free medium as "checks" upon the sugar-containing cultures.

In the first series of cultures, which were merely preliminary, the organisms were allowed to grow at a temperature of 37° C. until a maximum of pigment was developed. This time varied from seven to fourteen days. At the end of this time the cultures were sterilized and tested for sugar at leisure. Speaking generally, the results were that the pigment developed sooner in sugar-free bouillon and appeared earlier in the 1 per cent. sugar media than in the 2 per cent. media. The growth in itself was more rapid and luxuriant in the sugar-containing media, and at the end of the period of growth no sugar could be appreciated by Fehling's solution in glucose and lactose cultures, but some reduction did take place after inversion in saccharose cultures.

In the second set of cultures the same materials and the same organisms were used, but a temperature of 25° C. was adopted as a temperature best suited to B. pyocyaneus and B. prodigiosus at the same time. The cultures were allowed to grow not longer than seventy-two hours. One set was sterilized at the end of twenty-four hours, one at the end of forty-eight hours and one at the end of seventy-two hours. The results were as follows:

(In the following tables an × represents the smallest amount of color in growth present in the three cultures on the same line. A zero means total absence of color. An "S" in a subdivision of a column means that in testing with Fehling solution after sterilization, sugar was present. A zero in a like place means absence of sugar.)

CULTURES STERILIZED AT THE END OF 24 HOURS.

Organism.		Plain.	Glucose, 1%.		Glucose, 2%.	
B. pyocyaneus	Pigment.	× ×	×		0	
	Reaction.	alk.	acid	S	acid	S
	Growth.	×	× ×		× × ×	
B. prodigiosus	Pigment.	0	0		0	
	Reaction.	alk.	acid	S	acid	S
	Growth.	×	× ×		× ×	
B. janthinus	Pigment.	0	0		0	
	Reaction.	alk.	acid	S	acid	S
	Growth.	×	× ×		×	
B. fluorescens	Pigment.	0	0		0	
	Reaction.	alk.	acid	S	acid	S
	Growth.	×	×		× ×	

CULTURES STERILIZED AT THE END OF 48 HOURS.

Organism.		Plain.	Glucose, 1%.		Glucose, 2%.	
B. pyocyaneus	Pigment.	× ×	×		0	
	Reaction.	alk.	alk.	S	alk.	S
	Growth.	×	× ×		× ×	
B prodigiosus	Pigment.	0	0		0	
	Reaction.	alk.	ac.	0	ac.	S
	Growth.	×	× ×		× ×	
B. janthinus	Pigment.	0	0		0	
	Reaction.	alk.	ac.	S	ac.	S
	Growth.	×	× ×		×	
B. fluorescens	Pigment.	0	0		0	
	Reaction.	alk.	alk.	S	acid	S
	Growth.	× ×	× ×		× × ×	

CULTURES STERILIZED AT THE END OF 72 HOURS.

Organism.		Plain.	Glucose, 1%.		Glucose, 2%.	
B. pyocyaneus	Pigment.	× ×	×		×	
	Reaction.	alk.	alk.	0	alk.	0
	Growth.	×	× ×		× ×	
B. prodigiosus	Pigment.	× × ×	×		×	
	Reaction.	alk.	alk.	0	alk.	0
	Growth.	×	×		×	
B. janthinus	Pigment.	×	× ×		× × ×	
	Reaction.	alk.	alk.	0	alk.	0
	Growth.	×	×		×	
B. fluorescens	Pigment.	× ×	×		× ×	
	Reaction.	alk.	alk.	0	alk.	0
	Growth.	×	×		×	

(In these tables it will be noticed that glucose media alone were noted because it was impossible to make differential tests for the various products of decomposition of the complex sugars in the presence of each other, and so to give reliable results.)

From the above tables the following conclusions can be drawn: 1. That pigment is produced more readily in sugar-free media. 2. That growth is more luxuriant in sugar-containing media. 3. That pigment is produced earlier in 1 per cent. glucose media than in 2 per cent. media.

Cultures in media containing lactose and saccharose as well as those containing glucose give evidence that glucose offers the best nutritive advantages, that lactose is less readily used, and that saccharose is only with difficulty made use of by all of the bacilli with the exception of B. prodigiosus which seems to thrive equally well in all.

CHRONIC MALARIAL NEPHRITIS, WITH REPORT OF A CASE.

BY CHARLES W. LARNED, M. D.

(*Assistant Physician to the Dispensary, The Johns Hopkins Hospital.*)

The two points of greatest interest in the case I have to report are, (1) the fact that the infection was of the quartan type, the rarest of the three recognized forms of malarial fever, having been noted in but about 8 per cent. of cases recorded in this institution, and (2) the associated nephritis which was almost certainly dependent upon this or a previous malarial infection. The only other possible predisposing cause was to be sought in an attack of measles during April, 1898. This however can be ruled out, since the attending physician states that the attack was light, and that there were no symptoms whatever suggesting involvement of the kidneys, and especially when we take into consideration the infrequency of measles compared with malarial fever in this locality as an etiological factor in nephritis.

As to the connection between measles and a consequent nephritis, the following citations are of interest: Tirard[1] says, "It is comparatively rare for albuminuria to be associated with measles, and there is reason for suspecting that some of the cases which have been described under this heading were really cases of scarlatinal nephritis." Blum[2] in a collection of 45 cases of measles records but one that showed any renal involvement. Carr[3] collected at the Infants' and Children's Hospital, Randall's Island, 107 cases of measles, only one of which showed a nephritis, the condition being associated also with broncho-pneumonia with purulent infiltration, emphysema and pleurisy. Albutt[4] in London, where malarial fever is so uncommon, has collected 136 cases of nephritis due to all causes; of these, he attributes 3 to measles and one to malarial fever and exposure. Smith,[5] Goodhart,[6] Ashby and Wright,[7] Tyson,[8] Osler,[9] Anders,[10] and others, conclude that nephritis, if it ever occurs as a complication of measles, is exceedingly rare in this connection. Holt[11] has never seen a severe degree of nephritis associated with measles either clinically or at autopsy.

On the other hand malarial fever as an important factor in the production of nephritis has been recognized for a long time. The statistics at the Johns Hopkins Hospital, compiled by Thayer, and published in a recent monograph "On Nephritis of Malarial Origin," show that in 758 cases of malarial fever

treated in the wards, there were 21 instances of acute nephritis; of this number 11 recovered, 4 died, and in 6 the result was unknown. In four instances Thayer believes the process may have assumed a chronic form. He also states (page 23) that, "Out of 112 instances of acute nephritis observed in the Johns Hopkins Hospital, 21, or 18.7 per cent., were of malarial origin." He does not mention measles as a predisposing cause, although he gives statistics of cases of nephritis resulting from diphtheria, typhoid fever and scarlet fever.

Charcot[12] says that the albuminuria coincident with intermittent fever is at times transitory, augmented during the paroxysm, diminishing or disappearing entirely during the intermission, and ceases to exist the moment the fever is cured, or a short time after recovery . . . . . but that at other times the albuminuria persists a long time after the cessation of the paroxysms and takes on decidedly the chronic form.

Hertz[13] in speaking of albuminuria during malarial fever says "More frequently albumin is to be found after long-continued attacks of intermittent fever, or while a person is laboring under the malarial cachexia, and is then constant and quite abundant, depending upon the existence of an enlarged kidney or an amyloid degeneration of the renal vessels."

Rosenstein states that the dropsy and ascites accompanying nephritis of malarial origin attain a higher grade than in nephritis from any other cause.

Bartels[14] claims that next to chronic suppuration "Marsh Miasm" is the most frequent cause of chronic parenchymatous nephritis. He also thinks it may produce this condition without having been attended necessarily by paroxysms of any degree of intensity.

Tirard[15] holds rather uncertain views on this subject, stating that the influence of malaria as an etiological factor in chronic nephritis is open to considerable doubt. Further on he says "It must be admitted also that observations made in Algiers and Bombay show that in these places the association of chronic Bright's disease with malaria is as marked as it is in colder climates; hence the supposition that malarial nephritis is essentially due to exposure to cold scarcely seems to be tenable."

The pathological changes occurring in the kidneys during this disease have been studied by Bignami,[16] Barker,[17] Bastianelli,[18] Laveran,[19] Kelsch and Kiéner,[20] Rem Picci[21] and others.

Kiéner[22] in 1877, seems to have been the first to have worked up the histology with any degree of method; later in 1881 and 1889,[23] in conjunction with Kelsch, the same author did excellent work in this field. In their former work (pp. 279 and 495) they do not identify any particular form of chronic nephritis as the result of the malarial poison, the tissues reacting in the same way as to any other morbid impression, the process not confining itself to either the connective tissue or the secreting portions of the gland, the picture presented being that of a diffuse nephritis. At first the glomeruli and epithelium suffer most, the connective tissue being affected later. This however they do not claim as a fixed rule.

In their later work (page 276) besides going extensively into the pathological anatomy both microscopically and macroscopically they give at length the clinical aspects of the disease. Their conclusions are to the effect that this form of nephritis may be insidious during the course of a chronic malaria and discovered unexpectedly at the autopsy. At other times eclampsia finally reveals very suddenly a lesion already far advanced. In certain cases the symptoms are those attributable to an acute parenchymatous nephritis with anasarca, sudden, considerable and of rapid development, with scanty high-colored and bloody urine. In other cases the urine is clear, slightly albuminous, containing a few hyaline casts.

The consensus of opinion expressed by the different observers of the acute form seems to be that the pathological changes are not great, there being some pigmentation of the glomeruli with albuminous exudates and casts, the epithelium of the convoluted tubules being more or less swollen and degenerated.

Charcot[24] thought that the pigmentary alteration of the cortical substance might possibly be regarded among the organic causes of the persistent albuminuria.

The history of my case is as follows:

M. B., female. Age 7 years 5 mos. Colored. Complains of swelling of the abdomen.

Family History.—Negative.

Past History.—Child has never been strong, but has escaped the diseases incident to childhood, with the exception of measles, which she had during April, 1898.

In July or August of 1895, '96 and '97, the child visited Prince George's county, Maryland, and upon each occasion contracted chills and fever; the attacks were cut short and apparently cured by the administration of quinine, the paroxysms occurring each day, the chill and fever being quite marked.

The *present illness* dates back to July, 1898, when patient visited Anne Arundel county, Maryland. She commenced feeling badly while there, but did not have marked malarial paroxysms, only an occasional fever and sweat. On her return to Baltimore, at the end of two weeks, the grandmother noticed that the child's face was much fuller than when she left; in fact she thought the child was looking remarkably well. She attached no significance to the swelling till the abdomen commenced to enlarge; she then took her to one of the hospital dispensaries where a careful abdominal examination was made, but neither the urine nor the blood was examined. She was prescribed for, but the condition gradually grew worse, the abdomen becoming so distended that the patient could no longer be carried to and from the hospital. It was at this time, September 24th, that I first saw the child. I found her intensely weak; she could not turn in bed without assistance; there was no headache; appetite fair; no nose bleed, no herpes; slight cough; no pain in back or limbs; bowels loose since taking medicine prescribed at dispensary.

Physical examination showed marked œdema of the face, genitalia and ankles. Abdomen very much distended, tense, and exhibiting the usual signs of ascites; teeth irregular and notched but no pegging; tibiæ rickety; the heart's action was rapid, 128 per minute, forcible, apex not displaced, no murmurs; slight accentuation of aortic and pulmonic second. Lungs gave crackling râles over both bases with marked puerile breathing everywhere; respiration 46 per minute, thoracic in character, temperature 99° F.

The same evening I did a paracentesis abdominis, removing three quarts of turbid fluid, after which abdominal palpation

showed plainly the edge of the spleen about 5 cm. below the costal margin; the liver was not palpable. Suspecting malarial fever, treatment was deferred until the following morning when an examination of the fresh blood was made. This showed one or more intracellular parasites to nearly every field, the infected cells being decidedly smaller than normal, the organism occupying nearly the whole if not the entire corpuscle, the part remaining being greenish and easily discernible. The parasites were quite refractile, the pigment coarse, the granules not numerous, without motion, collected at the periphery and in many instances at the centre. There were many typical segmenting organisms seen, the number of segments ranging from seven to twelve; also one oval form. There were no hyaline forms noted.

This examination was made about 10 A. M., and when the child was seen, about 5 P. M., her temperature was 104.2°. I was prevented from making any further blood examination for three days, quinine being given in 4-grain doses during the interim. The parasites had then disappeared from the cutaneous circulation with the exception of an occasional atypical contracted form, pigmented leucocytes being quite numerous; a leucocyte in process of surrounding a small extracellular pigmented organism was noted.

The urine was light amber, slightly cloudy, acid, sp. gr. 1010. On boiling, almost a solid precipitate was thrown down; Esbach's albuminometer showed 2.1 per cent. albumin.

Microscopically there were hyaline, fine and coarsely granular, also epithelial casts, a great deal of detritus, no red cells, a few leucocytes and epithelial cells.

Fleischl's hæmoglobinometer showed 35 per ct. hæmoglobin.

Upon questioning members of the family further, a history of fever on every fourth day was easily obtained. The absence of chills and the fact that the child had been feverish only occasionally had not led them to suspect a malarial infection.

The treatment instituted was essentially, quinine, Blaud's pills, and later, Basham's mixture or bitartrate of potash; restricted diet and rather free purging. The child's condition improved steadily, the œdema rapidly disappearing; the hæmoglobin when last taken, October 15th, was 65 per cent. The amount of albumin, however, was always high, never going below $\frac{4}{10}$ per cent.; the specific gravity remaining in the neighborhood of 1010. The total amount of urine in 24 hours could not be estimated owing to constant action of bowels.

From October 15th to March 5th, 1899, I saw nothing of patient. On the latter date I was summoned at 10 A. M. and found the child profoundly comatose, pulse 160; she had had several convulsions during the previous five hours; her condition up till the day before had been considered good by the parents. Morphine, chloral, bromide and chloroform were administered with but little effect upon the convulsions, death occurring at 2.30 P. M. An examination of the blood just previously failed to show parasites.

Autopsy.—A partial autopsy only was granted, a member of the family remaining in the room. Notes taken just after are as follows:

3.30 P. M. Rigor mortis quite marked. Poorly nourished. Small for age. Rickety. Slight œdema of face and ankles. Abdomen distended, apparently by gas.

Abdominal incision showed marked agglutination of intestines, so much so that in getting back to the kidneys the gut was torn in several places. Edge of liver was not below costal margin; spleen extended about 2 cm. below costal margin; surface rather granular.

Kidneys slightly larger than normal, soft, capsule not adherent, surface rather granular, of a pinkish grey color, studded here and there with dots suggestive of fat. On section these same yellowish dots are noted. Cortex somewhat translucent. Striation not at all well marked. Glomeruli indistinct.

Dr. MacCallum who hardened and prepared the sections gives the following report:

Microscopically the kidney presents the picture of a chronic diffuse nephritis of the interstitial type. The glomeruli are extensively obliterated by an ingrowth of connective tissue along the vessels or by a thickening of the capsule. In the section a few are relatively normal, and in nearly all the capsular epithelium is fairly well preserved.

The connective tissue growth is quite diffuse, and the urinary tubules are generally compressed and atrophied. The well-known appearance of dilatation of the tubules in certain areas with flattening of their lining epithelium is present. Such dilated tubules contain masses of granular, colloid or hyaline material mixed with a few leucocytes and desquamated epithelial cells.

The tubules in general show flattening of the epithelium and evidences of degeneration in the epithelial cells. Many are desquamated into the tubules which in places contain a considerable number of polymorphonuclear leucocytes. Fatty degeneration of the cells is not, however, so extensive as one might expect. There seems to be a good deal of fat in the interstitial connective-tissue cells.

The blood-vessels show an extensive endarteritis.

CONCLUSIONS.

The conclusions to be drawn from this and other cases already on record, especially Thayer's and those of Kelsch and Kiéner, are:

1st. Certainly in some localities malarial fever should be given a prominent position in the etiology of chronic as well as of acute nephritis.

2d. In all cases of malarial fever the urine should be closely watched.

3d. A blood examination should be made in all cases of nephritis occurring in those who have visited or lived in a malarial district, as it often happens that the severe grade of nephritis resulting may mask entirely the clinical picture of malarial fever.

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A CASE IN WHICH THE BACILLUS AEROGENES CAPSULATUS WAS REPEATEDLY ISOLATED FROM THE CIRCULATION DURING LIFE.

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The generalized distribution of the bacillus aerogenes capsulatus throughout the body, as seen at autopsy, is usually ascribed to a pre-agonal dissemination from a local lesion or other source, and the recognition of the condition has so far been post mortem; the case of Graham, Stewart and Baldwin shows that the organism invading the general circulation may produce characteristic lesions in the tissues several hours before death; in this instance there had occurred an abortion and subsequent infection of the uterus, from which point the general infection proceeded. It is possible that in the living tissues of a subject presenting no local lesion, and whose resistance to infection has not been completely lost, the gas-producing and other functions of an organism may be more or less inhibited and the nature of the infection not become evident. The following case was probably influenced by these conditions, for although the B. aerogenes capsulatus was repeatedly demonstrated during life, none of the characteristic evidences of its presence as seen post mortem were to be made out.

The case, diagnosed as chorea insaniens, gave this history:

Alice B., white, aged 18, school-girl. Admitted May 13, 1899, complaining of St. Vitus's dance; family history, negative; had most of childhood's illnesses, and when 9 years old had mild chorea, from which she completely recovered without subsequent heart or joint symptoms.

Two weeks before admission she had been suffering from insomnia, extreme restlessness and nervousness; a few days later she was said to have been in a condition of severe nervous prostration and was sent home from school. On the way home she suffered from delusions of persecutions, imagining that the passengers would injure her. She showed great incoördination in her gait, reeling from side to side, tossing head and arms about and contorting her face. Her speech was slow, but intelligible. She grew rapidly worse, and by May 12 apparently every voluntary muscle of the trunk, face and limbs was affected, she being unable to talk or to feed herself. On admission she was unable to walk, was unintelligible in talk and quite out of her mind. There were ceaseless involuntary purposeless movements of muscles of face, limbs and trunk, the patient tossing and throwing arms and legs about, muttering and gibbering. There were no joint symptoms; no complaint of pain anywhere; no subcutaneous fibroid nodules; some erythema of elbows and knees from constant friction. Her pulse was regular, rapid, from 100–120. At apex of heart a slight thrill with systole was to be felt. On auscultation merely a booming, first sound, an accentuated pulmonic second sound and a soft systolic murmur over the pulmonary area were heard. There was no pericardial friction.

Her respiration was irregular, partly owing to irregular contractions of abdominal wall; lungs clear; knee-jerks exaggerated; no ankle clonus; plantar reflex present.

Patient improved for first few days after entry; facial movements became decidedly less and her mental condition clearer; the movements of trunk and limbs persisted. During this time her daily temperature had been ranging from 99° to 100° F., the nightly record being often higher, but in order not to interrupt the effects of sedatives was not regularly recorded. Stools and urine were voided involuntarily; in the latter a trace of albumen and a few casts were to be found.

After a few days of apparent improvement her symptoms became exaggerated; the temperature rose to 101.5°–101.7° on May 25 and 27; her pulse became more rapid and weaker. By May 28 her temperature was ranging between 103°–104° F. Her mouth and tongue were dry and fissured, the movements much more marked. Patient began to show signs of extreme exhaustion from ceaseless rolling and tossing. On June 3 she passed into a semi-comatose condition, remaining so till death, on June 6, on which date her temperature reached 106.5°.

A few hours before her death, a large, painful swelling of the right parotid was observed. There was no redness of the overlying skin, no fluctuation and no emphysema. No subcutaneous emphysema was to be felt over the body before or at death; after eight hours in ice-chest there were no alterations to be observed. Unfortunately, no autopsy was obtained.

The rapidly fatal course of this case and the concurrent symptoms suggested at once the presence of an infective agent, and cultures were repeatedly taken to determine its presence; the long-considered connection between rheumatism and chorea induced us to make use of the methods employed in the demonstration of the bacillus of Achalme, described recently by Achalme, Thiroloix and Savchenko in cases of rheumatic fever.

On May 16, 22, 24 and 27, and June 6 cultures were taken

from a vein of the fold of the elbow, 30–50 cc. of blood being extracted and distributed in different media.

Cultures of May 16. Aerobic cultures in bouillon and on agar plates and anaerobic in milk and bouillon mixture remained sterile. The cultures of May 22, 24 and 27 were made anaerobically in mixtures of milk and bouillon as recommended by the above observers, tubes of the same lot of media, and cultures from other patients in the same media being employed as controls; to further guard against error, an examination of the fresh blood for organisms was systematically pursued, and on two occasions several distinct bacilli resembling, morphologically, the bacillus to be described could be demonstrated.

All control tubes remained persistently sterile. Pure cultures of a large, non-motile bacillus were obtained from the patient on May 22 and 24, but a failure in obtaining anaerobic condition in the Buchner jar probably interfered with the development of bacilli on May 27. Although the sterility of the control tubes, the presence on two occasions of the same organism and its demonstration in the fresh blood were quite convincing, it may be objected that cultures in fluid media give chances of accidental contamination, and further that no idea of the number of organisms present is obtained. On these grounds, subsequent cultures on June 6 were controlled by the plate method.

As a rule, 5–10 cc. of blood were placed in each tube or plate. After 12–18 hours in Buchner jar at 37°, the inoculated tubes of milk and bouillon showed evidences of a very vigorous bacterial development: on the surface, a pinkish, fissured, firm, retracted clot: clinging to the sides of the tube clots also fissured, and containing gas bubbles, which, rising continually to the surface, formed there a frothy layer. The fluid in the tube had assumed a port-wine color, becoming black on exposure to air. The clot of blood was completely disintegrated, and an aromatic cheesy odor could be detected.

On glucose agar plates after 12–18 hours, 12 small, irregular colonies were visible, which after 48 hours were 1–2 mm. in diameter, gray-brown, with irregular margins, occasionally showing a central dot. An occasional gas bubble was to be seen about some. Numerous colonies of streptococci were also present at the last culture inoculation.

Microscopically, both in fluid and solid media the growth was found to be a large non-motile bacillus 8–10 μ in length, about 2 μ in width, very regular in size, with rounded ends, occurring singly or joined in pairs, often at an obtuse angle; rarely were more than 3–4 organisms seen in chains: an appearance as of a capsule was to be seen, which was subsequently demonstrated in experiments. The bacillus stained well by Gram; aerobic growth on the ordinary media did not occur, development taking place only anaerobically or in hydrogen. On agar slants small separate and fused gray-white colonies with somewhat irregular dentate margins were to be seen, an occasional gas bubble developing at bottom of tube.

Glucose agar was regularly broken up, and segments of the media were forced up the tube by the pressure of gas, some fluid appearing on top and in the spaces formed below.

In litmus milk and bouillon, gas formation was shown by the presence of numerous frothy bubbles on surface; in the former, in 18–24 hours, were to be seen fissured and retracted clots in a whey-like fluid, the clots, at first white from decolorization by hydrogen, becoming pink on exposure to air, thus indicating an acid reaction. The bouillon showed general cloudiness with a stringy, yellowish precipitate. Potato gave a scarcely visible film, often with gas formation in fluid below. Gelatin allowed a slow growth with production of gas bubbles and a general softening of the media; no complete liquefaction.

On blood serum (Loeffler) small isolated growths or a film of fused colonies, gray-white in color, developed. An odor of stale glue was noticeable, especially from the growth on solid media. A most abundant growth was always to be obtained in mixtures of milk, bouillon and serous fluid or blood. Under these conditions it could be repeatedly shown that development in presence of oxygen was possible. A standard culture of bacillus aerogenes capsulatus lent me by Dr. Harris responded to the same test. Further aerobic development in transplants on other media from these tubes has so far not been obtained.

Greater regularity of size of the organisms was observed in the young cultures on agar and blood serum; in fluid media short forms and chains appeared, the latter after several days' growth extending over several fields of the microscope; interesting involution forms were often to be seen on surface growths, irregularly staining, dentated, swollen or club-shaped bacilli.

Spores, usually centrally situated, oval, $\frac{1}{4}$–$\frac{1}{2}$ length of containing bacillus, were found on blood serum inoculated from a several days' old milk-tube; occasional end spores were also demonstrated; little swelling of the body of the bacillus was caused by their presence.

Continued transplantation of the organism tended to diminish slightly its size and regularity, smaller diplo-bacillus forms appearing in large numbers; occasionally in media to which blood or serous fluid had been added distinct capsules were to be demonstrated. Experimental inoculations proved that rabbits were insusceptible to intravenous injections of as much as 5–10 cc. of actively-growing culture. Killing the animal 3–5 minutes after the injection and keeping the body at room temperature showed enormous gas development in 4–8 hours. The subcutaneous emphysema, the condition of the liver and other organs, the presence of gas in the heart and vessels, serous cavities and tissues as described by Welch, Nuttall, and Flexner being accurately reproduced.

A slight detonation accompanied the ignition of the gas, which burnt with pale blue flame. Organisms in abundance showing distinct capsules could be obtained in pure cultures from the blood and tissues.

Guinea-pigs were killed in from 36–48 hours after subcutaneous injection. At site of inoculation characteristic lesions were produced, extensive œdematous infiltration of tissues with exudation of bloody serous fluid; in one animal the pericardium was found filled with fluid, evidently an extension of the œdematous process. Numerous bacilli, fibrin flakes and cellular elements containing organisms were present in the exudate; in most inoculations slight gas formation evidenced by emphysematous crackling was noted; in others it was perhaps too slight to be observed; necrosis and rupture of overlying skin were frequently seen.

In pigeons death ensued in shorter time, 24–36 hours. At site of inoculation some slight emphysema could be felt, which, however, might have been post mortem; œdema and sero-sanguinolent exudation with brownish-red discoloration and softening of the muscles were produced. Bacilli in numbers were present in the lesions. Depending upon the time elapsing before autopsy, greater or less numbers of bacilli could be detected in the blood and organs of the guinea-pigs and pigeons.

This resumé of cultural and experimental reactions seems sufficient to show that the organism is identical with the bacillus aerogenes capsulatus of Welch and Nuttall. The cultures obtained on three occasions corresponded accurately, and illustrate the possibility of a long continued infection by this organism, the first positive result being 13 days before death.

The gas-forming property of the bacillus, when in the circulation, may apparently remain in abeyance during the life of the infected individual; the duration of the infection, the seeming abundance of the infecting agent as evidenced by their demonstration in the fresh blood, and the fact that a general streptococcus invasion helped to produce the fatal ending, indicate but a limited degree of virulence on the part of the organism.

It is not assumed that the infection with the bacillus aerogenes capsulatus bears any etiological relation to chorea insaniens, the affection diagnosed in this case, but the bacterial association is of interest in connection with the acute infectious character this disease often presents.

According to Dr. Welch, to whom I am indebted for valuable suggestions, this is the only instance in which the bacillus aerogenes capsulatus has been demonstrated in the circulation during life; whether present as a primary or secondary infective agent is yet to be decided.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Monday, March 6, 1899.

Remarks upon a Case of Jejunal Fistula.—Dr. Cushing.

Surgical No. 8025. The patient, Lawrence L., from North Carolina, aged 28, entered Dr. Halsted's service on the 17th of August, 1898, with the history of having received ten years previously a razor cut across the abdomen which had completely severed the intestine in one place and had opened it in two others.

As a result of this injury from which he had made a marvelous recovery, an intestinal fistula, which was practically complete and which had resisted a subsequent operative attempt at closure, had persisted in the abdominal wall. On several occasions he had nearly starved to death from periods of inability to assimilate sufficient nourishment from the ingesta before it was lost through this accidental enterostomy wound.

His appearance on admission was most extraordinary. He was a man of large frame, emaciated to a degree and weighing only 93 pounds. His abdomen and thighs were covered with an acute brilliant dermatitis, which extended from the costal margins almost to his knees resultant to the irritating, continuous discharge from the fistula, which was situated in the median line below the umbilicus. To the right of this in the scar which extended almost across the whole abdomen there protruded a large ventral hernia (cf. photograph) through a transverse separation of the parietes about six centimetres in width.

The coils of intestine in this hernia showed a more or less constant visible peristalsis, and from the fistula, through which a rosette of mucous membrane usually protruded, issued in jets an acid, irritating and frequently bile-stained fluid. The skin everywhere in the vicinity was raw and thickened and so tender it could not be touched. The patient's mental condition, possibly as a result of his chronic starvation, was unbalanced and he had several epileptiform convulsions during his first days in the hospital, and the history mentions the occurrence of similar attacks during the past few years.

He was put in a continuous bath and was fed with nutrient enemata. Attempts to feed through the fistula were unsuccessful. The condition of the skin under water cleared up rapidly and he began to gain in weight under the rectal feeding.

Some months later he was operated upon; the fistula was closed by a resection of the bowel and end-to-end suture over a Halsted inflated rubber cylinder. The adherent coils of intestine were freed from the hernia sac with difficulty, necessitating another partial resection at one place. The abdominal wall was closed without drainage after excision of that part of the parietes involved in the hernia.

His convalescence was uninterrupted. His weight, 180 pounds to-day, has almost doubled itself since the operation. He gained eleven pounds in one week shortly after the operation.

The case presented many opportunities for physiological study, some of the results of which will be briefly mentioned here.

The *situation of the fistula* was evidently high up in the alimentary canal as was evidenced by the irritation produced upon the skin by the discharges.

It has been a common observation that the degree of dermatitis surrounding an intestinal fistula becomes more pronounced as the situation of the opening approaches the duodenum. The usual colostomy made in the large bowel causes no cutaneous irritation. It seems not unlikely that the pancreatic juice is chiefly responsible for this condition, as no fistulæ are so intensely irritating to the skin as those produced by opening and draining pancreatic cysts which have retained some communication with the secreting gland. In two other cases of high fistula now present in the wards, it has been necessary to place the patients in a continuous bath to control this acute eroding dermatitis. One was the result of a temporary fistula at the site of suture following a pylorectomy for carcinoma; the other was resultant to the establishment of a jejunostomy for post-operative obstruction. Biliary fistulæ are unirritating. Gastric fistulæ are commonly not followed by cutaneous inflammation.



December, 1898, weight 93 lbs.



February, 1899, weight 178½ lbs.

Surgical No. 8025. *Case of Jejunal Fistula and Ventral Hernia.*

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A method of determining the *exact distance of the fistula from the stomach* was suggested by the accidental discovery that oysters were discharged from the opening a short time after ingestion, practically unchanged. A piece of ligature silk was sewed through one of these before it was swallowed and three hours later the oyster appeared at the fistula. On careful measurement it was found that 3 feet 11 inches of string reached from the patient's teeth to the fistula. Peristaltic action was so strong and tugged at the string so vigorously after the oyster had been expelled that the patient had tied the buccal end of it about a lead pencil, which he was wearing between his teeth like a bit to prevent the string's disappearance. This measurement showed the fistula to be high in the jejunum, possibly one foot below the duodenum.

Physical examination of the stomach showed that there was no dilatation despite the extraordinary amounts of food, solid and liquid, with which the patient was accustomed to gorge himself at frequent intervals. Naturally a condition of chronic gastritis was present and the stomach contents after test meals showed great variability on chemical examinations. The reaction was always acid, sometimes due to free HCl, sometimes when this was absent, to fatty acids. This lack of constancy in the analysis of the gastric secretions unfortunately led to some variability in the results of many of our observations.

The *propulsive power* of the stomach and intestine above the fistula was very great. A glass of milk given on an empty stomach on one occasion began to appear, acid in reaction and finely coagulated, at the fistula in one minute and had been entirely recovered in four minutes. This rapid emptying of the stomach seemed most extraordinary. The patient had learned to prevent this immediate loss of food by swallowing large unmasticated pieces of meat and vegetables so that he would occasionally succeed in obstructing the pylorus and apparently at times the fistula itself, thus allowing of some absorption by the bowel above or possibly of some passage by the fistula. When the stomach was empty, peristalsis of the proximal bowel, seen through the thin parietes covering the hernia, was especially active and associated with "gnawing cramps" and the mucous membrane would protrude from the fistula to such an extent that on one occasion it became nearly strangulated when food had been withheld for 12 hours. (Cf. Photograph I.)

This motive activity was further shown by the fact that cold beverages would appear at the fistula before they had been warmed to the body temperature. A glass of ice water would reduce the temperature at the fistula a full degree while it was being discharged, and at such times the coils of intestine adherent in the hernial sac felt perceptibly cold to the hand.

Attempts to determine the *absorptive power* of the stomach were unsatisfactory. The fistula was too tender to allow the wearing of any apparatus to collect the discharge. Under ordinary circumstances when the stomach was empty there seemed to be no diminution whatever in the fluids collected from the quantity taken into the stomach. Whether there was some absorption when the bowel or fistula was blocked with food could not be certified.

The *reaction* at the fistula despite its proximity to the pancreatic ducts was quite uniformly acid, increasing in degree during digestion. It was due largely to the presence of fatty acid.

Some observations of great interest were made with Dr. Clopton on the *bacteriology* of the contents of the bowel under various conditions. These will be published in full in a forthcoming paper on the flora of this part of the intestinal tract. The great variation of the gastric acidity, chiefly in HCl, unfortunately made these observations at times somewhat uncertain. During active digestion on a mixed diet the flora of the discharge showed great diversity of organisms. It was found that several varieties of pathogenic bacteria taken into the mouth in inoculated milk could be recovered readily and grown at the fistula. We also succeeded in demonstrating that the ingestion of a sterilized diet, the mouth meanwhile being rendered as clean as possible by frequent antiseptic washes, was followed by a pronounced diminution in the number of colonies on plates inoculated from the lumen of the proximal bowel. For forty-eight hours before the operation every precaution was taken to prevent the entrance of micro-organisms through the mouth, and, at the time of operation, cultures taken from that part of the bowel above the fistula, where a partial resection was rendered necessary, remained sterile, and no organisms could be demonstrated on stained preparations from the mucosa. Resection and "end-to-end" suture followed by closure of the parietes without drainage, under such circumstances, is attended with little risk.

I regard this as an all-important procedure, when time permits, in the preparation of a patient for a laparotomy during which the bowel is likely to be opened or when a resection and suture is premeditated. The results of observations in this direction during the past year will be published.

Treatment of Acute Otitis Media following Influenza.—Dr. Theobald.

I wish, to-night, to speak more especially of the abortive treatment of these cases when one can see them in the earliest stage.

There have been, as you probably know, an exceptional number of serious ear troubles following the influenza or grippe. The statistics bearing upon this subject that Dr. Bacon gives in his recently published treatise upon the ear are interesting. He says that a few years ago 12 to 20 cases of mastoid disease were about the average met with in the course of a year in the New York Eye and Ear Infirmary, while in 1897 there were 161 mastoid operations. He attributes this great increase to the prevalence of influenza.

The most serious involvements are those in which the brain is affected. This may happen in several ways. Epidural abscess is one of the more common forms, and purulent meningitis is another. Abscess of the brain substance itself or thrombosis of the lateral or sigmoid sinus are other ways in which the brain may be involved.

The modes of infection of the middle ear may be referred to in passing. The most common way is through the Eustachian tube. Nature has provided a means for lessening the likelihood of this happening, the ciliated epithelium of the Eustachian tube acting in such a way as to hinder the entrance of bacteria

from the nasal cavity into the middle ear, but it is only partially successful. Another route of infection is through a perforation in the tympanic membrane. The infection may occur also through the blood-vessels or the lymphatics.

Various micro-organisms have been found in suppurative middle ear inflammations. The staphylococcus aureus and albus, the streptococcus pyogenes and the pneumococcus are among the most common, the two first-named being found especially in the milder cases. The micro-organism that is supposed to be the cause of influenza is occasionally found, but is usually accompanied by other organisms. My own experience is, that the purulent infection occurs very frequently, only after perforation of the tympanic membrane. This is not always so, for often when the tympanic membrane is incised pus escapes; but not infrequently the discharge is not purulent but sero-mucoid, tinged with blood, and does not until later become purulent. It is a very difficult matter, even with antiseptic precautions, to prevent infection after a perforation has occurred or an incision has been made through the tympanic membrane, for one cannot sterilize the skin of the external auditory canal as thoroughly as the skin upon other parts of the body may be sterilized.

Every one is familiar with the symptoms of inflammation of the middle ear. Pain is the most prominent symptom, and deafness occurs, but the pain is so great as to prevent attention being called to the latter. Tinnitus aurium is usually present. The temperature, in children especially, is apt to run high. Even in uncomplicated cases in children it may reach 105°. In adults we are not apt to have so high a temperature unless there are serious complications.

In the beginning of the attack, if we inspect the ear with the mirror and speculum, we will see a hyperæmia of the upper part of the membrane, especially of Schrapnell's membrane, and running down the handle of the malleus will, perhaps, note a line of congested vessels. A little later, the whole membrane becomes red and loses its normal appearance. If the attack runs a little longer we shall usually find evidences of fluid in the tympanic cavity, causing bulging of the membrane, usually of the posterior and lower quadrant, but sometimes of the membrana flaccida.

What I want to speak of more particularly is the early treatment of these middle ear inflammations, especially of those cases following the grippe. I believe, in the large majority of instances, if we can see these cases early, that is, within a few hours of the onset of the pain, we can cut short the attack. I think it is greatly to be desired that this should be accomplished, for if the inflammation is not controlled promptly it is extremely difficult to prevent suppuration. Even when this occurs, most of these cases, it is true, do well; but we never know when serious complications may supervene.

I have recently met with the most rapid death following ear disease that I have ever encountered. The patient had had influenza, had been out and exposed to cold, and was taken on Friday with ear-ache. She suffered severe pain Friday night and Saturday and was given morphia liberally to relieve the pain. On Sunday she showed signs of nervousness and irritability, and when I saw her, for the first time, on Tuesday evening she was delirious, had a temperature of 105°, and a very rapid pulse, and a look into the eyes satisfied me that there was commencing optic neuritis.

There was no reason to suppose, in this case, that the mastoid process was involved, but it was evident that there had been a direct extension to the brain from the tympanum, and there was no doubt of the existence of a meningitis. An extensive operation upon the brain suggested itself as a possible means of relief and, at my suggestion, Dr. Finney saw the case, but he thought the condition of the patient was such that no operation was advisable, and she died on the following morning. This is an extreme instance of how rapidly ear disease may induce fatal brain complications. If, then, we can abort these cases, in which such a result is a possibility, it is most important to make the attempt and make it early. The plan of treatment which I recommended years ago, and for which I have been given considerable credit, although I do not deserve it, as the suggestion was not original with me, is the using in the ear of a solution of atropia, to which I have added more recently cocaine. I prescribe either a watery solution of atropiæ sulphate and cocaine muriate, or a solution of the alkaloids of atropia and cocaine in oil of sweet almonds. In either case the strength of the solution is half a grain of atropia and one grain of cocaine to the drachm. The advantage of the oily solution is that it remains in contact with the tympanic membrane for a longer time and so favors freer absorption, and further, if there is a perforation of the membrane present it is not so likely to find its way through the Eustachian tube to the throat and produce constitutional effects. When the solution is to be put into the ear the patient should lie down with the affected ear up, and should be kept in this position for at least ten minutes, so that the solution may remain upon the tympanic membrane. A little cotton can then be put in the ear and the head raised.

Eight drops of the solution, warmed (5 or 6 drops in the case of children), are used at a time. This means about 1-15 grain of atropia; but the absorption is very imperfect and there is no danger of constitutional effects from the application, unless a perforation of the membrane exists. Where this is the case, however, one should be a little cautious, and I always speak of the possibility of constitutional effects, and advise accordingly. The instillations may be repeated 3 or 4 times a day as long as pain is present. I have seen occasionally slight evidences of the systemic action of atropia from this plan of treatment, but never anything alarming. In addition to this local treatment I give small doses of calomel every hour or half hour until the bowels are freely moved, and if the effect of the calomel in this respect is slight I prescribe a saline cathartic.

The result of this plan of treatment, if only one sees the case in its incipiency, is usually extremely satisfactory. The pain is often relieved within a few hours and the inflammatory process controlled so effectually that in the majority of cases an incision of the membrane or a spontaneous perforation is avoided.

After the acute symptoms have subsided, the tinnitus and deafness which are apt to remain are benefited by liberal doses of muriate of ammonia—ten grains, three or four times a day. If the pain is not controlled by the cocaine and atropia instil-

lations, antikamnia or phenacetine may be administered, or, if necessary, morphia. It is not safe, of course, to wait indefinitely for the effects of this treatment; but my experience with it has been so favorable that I am sure I wait longer than many do before incising the tympanic membrane. If it is evident that the tympanum is distended with fluid a free incision should be made, preferably through the posterior portion of the membrane.

One does not make a small puncture, as was formerly advised, but a free incision, beginning it well up and carrying it down parallel with, and close to, the posterior margin of the membrane. After this the ear should be syringed with a saturated solution of boracic acid two or three times a day, and if this does not control the suppuration a solution of bichloride of mercury, 1 to 8000 to 1 to 4000, may be employed instead.

The effect upon the hearing in these cases is not usually disastrous. In the mastoid cases the impairment is often pronounced and permanent. In the milder suppurative cases, however, we expect a complete restoration of the hearing.

Dr. Reik.—I would like to add a few words to what Dr. Theobald has said concerning the treatment of these cases. As Dr. Theobald has already said, there has been a larger number of cases of otitis media accompanying or following the recent epidemic of grippe than has occurred in the past. I fully agree with the method of treatment he has outlined except that I am, perhaps, in favor of incising the drum membrane at an earlier stage.

Wishing, however, to avoid an operation wherever possible, I have frequently made use of local blood-letting in addition to the treatment described by Dr. Theobald. I apply one or two leeches over the mastoid region and allow the bleeding to continue for some time after their removal. It is remarkable in many cases to note the great relief that follows almost immediately upon their application. The pain ceases to such an extent that the patient soon falls asleep and the inflammation is retarded.

Dr. Theobald.—There can be no doubt of the value of local blood-letting in these cases.

Dr. Finney.—I saw the case Dr. Theobald referred to, a few hours after Dr. Theobald saw her. She was then comatose, with a pulse that could hardly be counted, a temperature of 105 to 106 degrees, very high, and utterly beyond operative aid.

There was at that time no evidence that would aid in the localization of the trouble. There had been no paralysis, no muscular contractions; the pupils were of the same size and there was no evidence of any trouble or any other evidence that I could detect by examination or the history of the case, that would aid in localizing the process, and even had we gotten any idea of the location of the trouble, I thought at that time, there would have been no use in operative interference.

I saw one other case, just a day or two before this one, that was similar in many respects, only of more happy termination. Also a young woman, sick for two or three days, had had grippe and recovered from that apparently, and a week later complained of headache which lasted for some time, only very intense she said, and always referred to right ear. After a few days she noticed a certain amount of discharge on the pillow in the morning, supposed to be from the ear, although the physician who saw her said he could find no discharge from the ear, nor was there any discharge from either ear that I could detect at the time I saw her. The drum upon that side was ruptured, she was stupid, dull, very different from the usual vivacious temperament. Could be roused enough to answer questions intelligently, but it required considerable effort to rouse her. Upon pressure over the mastoid she evinced some pain. No swelling or other evidence of mastoid trouble.

We thought it best to open the mastoid and did so and found no evidence of trouble so far as I could detect. I continued the opening in the bone until I exposed the lateral sinus and punctured that. It bled very vigorously and I came to the conclusion that the lateral sinus was not at any rate thrombosed. I drained the wound, and the patient from that time made a rapid recovery and is now entirely well.

Some Objections to the Neurone Theory.—Dr. Paton.

The investigations of Apáthy, Bethe and Nissl have shown that the ganglion cells in the spinal cord and brain contain a specific fibrillar substance essentially different from the protoplasm of the cell body and its processes. This substance can be stained by several different methods. Little is known of its origin. It may be shown to be an integral part of the ganglion cell or it may develop from other cells in the nervous system, or it has been suggested that it may be the product of both kinds of cells.

Until it has been determined histogenetically that the fibrillary substance is a part of the ganglion cell it is an assumption to speak of these cells as units or individuals. The picture of the ganglion cell, obtained by the use of Nissl's methylene-blue method, is the negative of that given by Bethe's new stain. The achromatic tracts in the first correspond to the colored tracts or fibrils in the second specimen. Nissl believes that the fibrillary substance is present, not only in the cells, but exists in large masses in the intercellular substance and is one of the important constituents of the grey substance.

In the main the fibrils follow the distribution of the dendrites and axons. The life of the fibrils undoubtedly depends upon the preservation of the myelin sheath. There is nothing revolutionary in the new discoveries in relation to the studies of the degeneration of nerves. Little has been done in studying degenerations. Bethe has cut peripheral nerves and found that the fibrils degenerated, and that in a short time there is nothing left but granular masses. There is a great deal of interesting work to be done on this subject. Nissl emphasizes the importance of the nerve cell as a nutritive centre. If later the fibrils are proved to develop in the nerve cell, and not from other cells, it will no longer be an assumption to speak of the nerve cell as a unit.

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A BIOGRAPHICAL SKETCH OF JOHN ARCHER, M. B.*

By One of his Descendants.

John Archer, M. B., was a son of Thomas Archer, a descendant of an English family that had settled in the north of Ireland; whence he emigrated to America with several brothers before the middle of the last century; and after a brief sojourn in Cecil county, Maryland, removed to what is now Harford (then part of Baltimore) county, where his son John was born near the present village of Churchville, on the 5th of May, 1741. Besides farming, Thomas Archer was agent for several extensive iron works in the vicinity. He also drew up indentures for his neighbors, auctioned off goods, etc., and thus acquired a considerable estate. Among his other enterprises, he set up, on his own premises, a skilled blacksmith, which, no doubt, gave rise to the false assertion that he himself worked at the trade. His wife, Elizabeth (Stevenson) Archer was also of an English family that had settled in the north of Ireland. Of their five children, four were swept off in their infancy by a malignant epidemic, the subject of this sketch barely escaping death from the same disease; and from him all of the name in Maryland who are in any degree whatever related to the family, are descended.

John Archer was educated in part at West Nottingham Academy, in Cecil county, a school of wide repute, in charge of Rev. Samuel Finley, a learned minister, its founder, who was subsequently called to the presidency of Princeton College. Among his classmates at this academy were two of Mrs. Finley's nephews, Dr. Benjamin Rush and his brother Judge Rush, with the former of whom he enjoyed a lifelong intimacy.

In 1760 John Archer graduated, A. B., at Princeton, and A. M., in 1763. Meanwhile, in February, 1762, he advertised that he would open a Grammar School in Baltimore Town. There is reason to believe, however, that this project was never initiated, as he soon afterwards entered upon the study of theology under Presbyterian auspices and progressed so far as to preach his trial sermon—which is, I believe, still extant—but, on being examined for ordination, he failed to pass the ordeal. The record of his examination by the Presbytery of New Castle is worth giving here in full, if for nothing else, as a specimen of human inconsistency as to the time-being, and fallibility as to the future. It runs to the following effect:

"30 Aug., 1764. Mr. John Archer having at last meeting of Presbetery offered himself for Tryals as a candidate for the sacred ministry, then delivered a discourse by way of specemine, on a text that had been assigned him. He was also examined at some length in the Latin, Greek & Hebrew languages, his own experience in religion & on some points of divinity; but the Pb'y not having time fully to satisfy themselves thought it best not to enter him

*Presented to the March (1899) Meeting of the Johns Hopkins Historical Club.

then on their minutes, & only recommended to him another subject for a discourse by way of specimine. Mr. Archer now delivered said discourse & was further examined on the article of experimental religion. The Pb'y upon solemnly considering the whole, do so far sustain his answers on the several Branches of Examination & particularly said Specimine, as to enter him upon further tryals, & appoint him to compose an exegesis upon the question, "*In quo fundatur obligatio moralis?*" [What is the basis of the moral obligation?] & a discourse on Romans VII. 15. ["For that which I do, I allow not: for what I would, that do I not: but what I hate, that do I."]

"6th Dec., 1764. The Pb'y proceeded to hear the exegesis given to Mr. Archer by our last, & further examined him on Logick, & asked him some questions on Divinity; & on the whole, unanimously judge that though we would gladly encourage youths who offer themselves for the sacred ministry yet think Mr. Archer through the whole course of his tryals discovers such a want of knowledge in divinity & the other particulars he has been examined on, as well as such an incapacity to communicate his ideas on any subject, y^{t} we cannot encourage him to prosecute his tryals for the Gospel ministry any further."

Now, it is evident from the record itself that the candidate, in the opinion of the Presbytery, was well versed in all the essential branches except as to some points of the denominational creed. And as to his "utter incapacity to communicate his ideas on any subject," it is a sufficient answer to say, that the Presbytery had just declared, as the record runs, that he was particularly satisfactory in his discourse or sermon before delivered.

Col. Nathaniel Ramsay, the hero of Monmouth, is authority for the statement that he was present when John Archer underwent his trial before the Presbytery; and that his failure of ordination was "because he did not give entire satisfaction on some doctrinal points."*

In the spring of 1765 he became a pupil of Dr. Morgan, who, in the following November, began the initiatory course of medical lectures in Philadelphia College, with Dr. Shippen as his colleague,—these two being the founders of the department of medicine in that institution, afterwards the University of Pennsylvania.

About this time he wrote as follows to his future wife:

". . . . I am daily at Dr. Morgan's shop, & on Mondays, Wednesdays & Fridays attend his Lectures—the Course is four Pistoles & a Dollar. Tuesdays, Thursdays & Saturday's Dr. Shippen's—the course, six Pistoles . . . . I have concluded to remain in Philadelphia until Spring come a year."

In February, 1767, he wrote to the same lady—then his wife—the following, which, as I believe no account of the case has ever appeared in print, may be of interest at present:

". . . . A monster was lately born in Charles Town [Cecil Co., Md.] in the shape of two negro children in one. They have two heads, four arms & four legs, distinctly & regularly formed; they are united from the shoulders to a little below the navels & lie in each others' arms, and each having its arm under the other's head. This wonder of nature is now in Town.—I saw it yesterday. It has been opened, & the bowels are distinct & separate, as in two infants, ought to be. One of them presented near half an hour to the world before the other & was alive at its first appearance. The midwife gave up the delivery, which was afterwards executed by the owner of the wench, who himself understood nothing of the business. The owner is John Kirkpatrick of Charles Town."

On the 6th April, 1767, he wrote to his wife:

". . . . It will be some time before I can go down [to Maryland.] Dr. Morgan's Lectures will not begin before May 20th, & I am determined to hear them to the last. Dr. Bond's will not begin until ye last of May.* However, I shall not wait for his. . . . . Dr. [Robert] Harris has taken Dr. Bayard as a partner in the drug business & Practice of Physic."†

April 21st, 1767, he writes to the same:

". . . . All prospect of entering into partnership with Dr. Boyd of Lancaster is vanished. Therefore I still have the wide world to seek where to pitch my tent."

In the summer of that year—between his second and third course of lectures—he proceeded to put into practice, among the denizens of New Castle County, Delaware, the professional knowledge which he had acquired. He, no doubt, gave this locality a temporary preference over the place of his nativity merely because it was much more convenient to Philadelphia, where his medical education was yet to be completed. His ledgers show that during his two years residence in Delaware he attended 212 families, receiving for his services about $1000, nearly three-fourths of it in money—the remainder in rent, produce or labor, including the work of mechanics. About one-third of them paid nothing at all. There is, in his ledger, kept while practising in Delaware, a prescription, which, though a little humiliating, it is the duty of the faithful biographer to record. It may perhaps be condoned, for the reasons that it is the only one of the kind in all his ledgers, and that it antedated his diploma—though, truth to say, only a few days.

The entry runs in this wise:

"Rev. Mr. Elihu Spencer Dr. 1768 June 6th
Milleped: pp^{t} for your Daughter."

This, of course, was to be taken in one dose; and there being no other prescription entered for that particular patient, though the attendance upon the family was quite extended, it is fair to infer that it either killed or cured. At that date such revolting prescriptions were nearly out of vogue, though once an every-day matter. Dr. Buckler Partridge, who came from England and practised in what is now Harford county, Md., from 1715 until about 1750, was wont to dose his unfortunate patients—as his prescription book still extant amply shows—not only with millepeds, but with "juleps of goat's blood," "powdered bees," and "dried viper's flesh"; and, as if these were not enough in themselves, his favorite vehicle for conveying them into the wretched patient's stomach, was a copious draught of nauseating "frog-spawn water." And yet Dr. Partridge was the leading physician of his day thereabouts. Even "Hooper's Medical Dictionary," a standard

* Col. Ramsay made this statement to my father, Dr. Robert H. Archer, one of John Archer's sons, who at that time was his family physician and who communicated it to me.

* Dr. Thomas Bond at this time delivered clinical lectures at the Pennsylvania Hospital. In May, 1768, he was elected to the chair of clinical medicine in the new institution.

† Dr. Robert Harris was a brother of Dr. John Archer's wife. He was a very prominent member of the profession.

work of only fifty years ago, contains the following prescription, which, for sheer loathsomeness may perhaps be said to exceed them all: "For very obstinate jaundice: The expressed juice of 40 or 50 living millepeds given in a mild drink."

After attending his third course of lectures—Dr. Kuhn having meanwhile been added to the faculty—the degree of Bachelor of Medicine was conferred upon him and nine other students on the 21st of June, 1768. This being the first occasion in America of the conferring of a medical degree, it was to be expected that even under ordinary circumstances some contention would arise as to who should be the recipient of the very first honor of the kind in the new world. Unfortunately in this particular case the decision was greatly complicated by the fact—which soon became known—that the faculty of the College, most of whom had been educated in England, wished to show their respect for the mother country by conferring the first diploma upon the only Englishman among the candidates—Jonathan Potts. But, with the recent attempted humiliations of the odious stamp-act fresh upon their memory, the glorious nine regarded this loyal concession as a downright insult. After a vain protest, they threatened to demand certificates of their successful examination,—armed with which, they would secure the coveted parchments from the neighboring College at Princeton. That settled the question. The thought of losing all except one of their graduating class, and he a foreigner, was more than the intensest loyalty could have endured. The rebels were told to arrange the matter among themselves. This they did by compromising upon the alphabetical order. It may seem a little strange that this was preferred to a decision by lot,—usually the fairest way in such cases. There is little doubt, however, that they were afraid a trial by lot might possibly give the prize to the Englishman, after all their contention; whereas, by the alphabetical plan, as they must have known at a glance, this was impossible. It is greatly to their credit, however, that they generously allowed him to come in several grades higher than he would have attained by the plan agreed upon if strictly observed,—the following being the order of graduation as given in the official catalogue: "John Archer; Benjamin Cowell; Samuel Duffield; Jonathan Potts; Jonathan Elmer; Humphrey Fullerton; David Jackson; John Lawrence; James Tilton; & Nicholas Way."

Declining an offer of partnership kindly extended to him by his preceptor, Prof. Morgan, Dr. Archer returned to his native county in July, 1769, where he practised his profession for nearly forty years. These duties, however, did not prevent him from taking part with characteristic energy in the great struggle for liberty. He was chosen in November, 1774, a member of the first local Revolutionary Committee and of the several successive committees, until August, 1776. Meanwhile, in December, 1774, he enrolled the first militia company of the county, was commissioned its Captain and drilled it regularly until called to other duties in the patriotic cause*—though forced to use a speaking-trumpet, his voice having been permanently reduced to a hoarse whisper by a severe throat disease. The sword which he wore on these occasions is still in possession of a branch of the family. But the trumpet is long since lost, or mouldered away. For many years his sons were wont, on every 4th of July, to bring it down from among the rubbish in the old garret of "Medical Hall" and make the premises ring with the re-awakened notes of Independence.

In January, 1776, he was commissioned Major of one of the local Battalions of Militia.

In August of the same year he was elected a member of the convention which framed the Constitution of the new State and the Bill of Rights.

In 1777 he was appointed one of the Commissioners of Peace for Harford county, who constituted the County Court, and held the office for thirteen years, when the court was reorganized on a different basis. During part of this time he was also one of the Judges of the Orphans' Court.

In November, 1776, he was chosen as an Elector of the State Senate—the senators being then chosen by an electoral college.

During all this time, as his medical ledgers, still extant, amply show, he practised his profession, not only throughout several counties of his native State, but also in the adjoining State of Pennsylvania.

After the Revolution he devoted himself exclusively to his professional duties. Facilities for acquiring a knowledge of the medical profession being then extremely meagre, students from far and near placed themselves under his tutorage. He built a substantial stone office a few steps from his residence, "Medical Hall," and for a quarter of a century it was seldom that half-a-dozen young men were not under his instruction, one or more of whom, after a certain course of reading, would accompany him on his tedious professional rounds, hearing from him veritable clinics at the bedside, and on their return compounding under his directions the necessary prescriptions. After a longer apprenticeship, he intrusted exclusively to their care the less obscure and complicated cases, whose symptoms they noted and reported to him. Indeed, but for their subsidiary aid, he could not possibly have done justice to one-half the patients under his care. In several of his ledgers the visits and prescriptions of his various students are noted by their initials. From 1790 to 1794 thirteen students are thus noted, most of whom were afterwards in active practice in various parts of the country. And there were probably others. His students formed the first medical society of Harford county, which met at stated periods in the office at "Medical Hall." Some of the papers read on these occasions are to be seen, in manuscript, in the library of the Medical and Chirurgical Faculty.

In 1797 he was chosen Presidential Elector at large on the Jefferson ticket.

He and his son, Dr. Thomas Archer, were charter members of the Medical and Chirurgical Faculty, January, 1799. In the following June he was chosen one of the Examiners; and in 1802 and 1803 was on the Executive Committee.

In May, 1799, he wrote,* " . . . . Some person without my

* I have often heard my father state the facts above given, which he had from his father, the subject of this sketch.

* All the letters quoted from in this sketch, unless otherwise noted, are addressed to the subject's son, Dr. Robert Harris Archer.

Knowledge hath published that I am a Candidate for the important Place of Elector of the President. It is not my Wish, as I am certain a popular Character in Baltimore county would have a greater Chance than I could be expected to have."

In 1800 he was elected a member of Congress; and two years later he was re-elected. While a member of that body the physicians of Washington and vicinity availed themselves of his professional advice in cases which had baffled their skill. It was at this period that he discovered the interesting fact, that in the early stages of whooping-cough, vaccination will so modify the disease that its course is rendered comparatively harmless, even in winter. He also contrived and used, in cases of fractured femur, the apparatus which afterwards became famous as "Physick's modification of Desault's apparatus."

On the expiration of his second congressional term he resumed the practice of medicine. But the following, from one of his letters written at the seat of government, in April, 1802, more than hints of the strong man's failing vigor: "I shall be a very valetudinarian, and in my old days begin to investigate what will best agree with me, who once knew no difference in any kind of diet; who could eat anything without fear that was suitable for nutrition. But those days are gone with the days before the Flood."

A few years later, partial paralysis, the sequel of an attack of rheumatism following a severe fall, unfitted him for the discharge of his professional duties. He relinquished all active pursuits and his health gradually declined. The end came on the 28th September, 1810, when he expired suddenly, in the 70th year of his age, at his home, while sitting in his easy chair,—an asthmatic ailment for some days before his death precluding a recumbent posture.

A marble slab over his grave in the burying-ground of the Presbyterian church at Churchville gives merely the dates of his birth and death. Of that church he was a member for nearly half a century.*

Extracts from a few of his letters (some two dozen of which are still extant, written in great haste, nearly all of them to his son Dr. Robert Harris Archer, then practising his profession in Baltimore), will give glimpses of him not only as a physician, but as a parent, a Christian, a patriot, and a politician. In a letter of date May 31, 1798, he advances the theory, that—

"While the country in this section, which I distinctly remember as far back as 1750, was covered with Oaks, Willows, Maples, Beeches, Alders, Chestnuts, etc., which are Astringent and Antiseptic, the rain which ran off from their Roots into the Streams & Swamps prevented Sickness, as Salt in the Ocean prevents it. And in proportion as the Country was denuded of these natural Antiseptics, Fevers prevailed. In other words they prevented Putrescence of both vegetables & Insects, which is the Cause of Remittent & Intermittent Fevers. . . . . Crowded & dirty Cities are nurseries of Putrefaction."

"July 12, 1798. . . . . The Physicians of Philadelphia & Baltimore now succeed in curing Croup with Rad. Senekæ, though the disease was before almost *opprobrium Medicorum*. But they are so obstinate, they will not acknowledge it, because they were not the first to discover the remedy. I was informed when in Philadelphia that Dr. Kuhn has not lost a Patient since he has used the Seneka. I would, before I close these observations, just remark that the cure could be expedited by dipping a cloth in a hot decoction of the Seneka, to be held frequently near the Patient's mouth & nose, that the vapor may be inhaled & come in contact with the membrana trachealis. This I would not communicate to any of the unbelieving gang—*Si volunt desipi, desipiantur*."

In a letter without date, but probably written in 1798, he says:

". . . . The proper time for repeating the Cortex Peruviana I have found from experience to be the 7th or 8th day. Dr. Moons [one of his former students], in his Thesis [at the University of Edinburgh], has not given me credit for this practice, as he should have done. It is not to be found in any practical work before that date, unless in a very vague way—no precision is determined—no time set apart for taking it, to counteract the Return of the Fever.

"This is a hasty scribble, & as such you will take it."

"Harford County, Sep. 4, 180.

". . . . I am of the opinion that the seat of the disease [yellow fever],* is in the primæ viæ—that the septic gas impregnates the saliva, water, & especially meats; that taken into the stomach it acts as a ferment, & according to the concentration of the Gas, is the violence of the Disease. Its state of concentration may in general be judged by the color of what is vomited & the Fœtor of the motions. The different degrees are *green, brown, coffee-coloured & black*. The nature of this Gas, from the experiments I have made, is an acid; therefore, this year I have exhibited Absorbents very freely by Glyster, with occasionally Laxatives & Laxative Glysters until the motions ceased to be fetid. I have given the Absorbents every two hours & ordered Glysters every four hours with the happiest effect. When the excessive stimulus is taken off the fever soon intermits & the Bark is given with the best results. The lowness of the Pulse is from the excess of the Stimulus in the Intestines; when this is corrected, the pulse becomes fuller. Bleeding, in some cases, may be advisable to lessen the effects of stimulus; otherwise, it is not indicated. When it is used very largely the Patient may die by great Debility. Cathartics are absolutely necessary, not only to remove the Septon, but to carry the Absorbents soon through the bowels. A large dose of Absorbents should be given with the Cathartic, & a Dose after every Motion. Care should be taken that the Patient does not become costive, as the Absorbents are apt to be formed into hard Excrements difficult to evacuate.

"I have not time to be more particular. I could show the rationality of this method—that it accords with Philosophic Principles. Should it succeed with you, it will give me Pleasure. It will be a new mode of treating the Fever; & the cause of the Fever will be better known."

His treatment nearly one hundred years ago, as above given, was almost identical with that so strongly recommended by recent writers,—among them Dr. Sternberg, Surgeon-General

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*Of him, Dr. Mitchell of New York, said: "He left the world full of years and full of honors. His life was fully devoted to the service of his fellow-creatures and to the glory of the great Redeemer. As a physician he was beloved in a peculiar manner by all who knew him. His early piety, ripening into maturity with his years, enabled him to meet death with persuasion of his acceptance with God."

*The son to whom this letter is addressed was at the time Physician to the special Yellow Fever Hospital in Baltimore, and narrowly escaped death from the disease a year or two later.

of the United States Army, who also expresses the same view of the nature of the disease: namely, that its seat is in the intestinal canal and that alkalies (absorbents) should be administered to neutralize the acids which favor the production of yellow fever germs.*

"Harford County, Sept. 19th, 1800.

"I am sorry to hear of the deplorable condition of Baltimore. . . . . We have had two or three cases of Yellow Fever that originated in the county, & two or three from Baltimore have died. One of them refused to take medicine. One of them was in a cold Sweat, & vomiting dark, coffee-coloured Bile; arms and legs with purple Spots—was cured with Absorbents, opium, laxatives & Bark—absorbents & Opium given very freely—laxatives to prevent Constipation, & Bark as a Tonic."

The following was also written in September, 1800:

" . . . . I am anxiously concerned for you, dwelling, as it were, in the midst of Death. Such chastisement by Divine Providence should lead the contemplative mind to God & our Saviour. . . . . I hope you will be careful to avoid bad company of all Sorts, & when time & the situation of your Patients will admit of it, you will, on Sundays, attend some place of Divine Worship. The neglect of our Worship of the Supreme Being is the forerunner of the Sinking of a good Moral Character. When the Attendance on the Duties required by the Christian Religion is neglected, there is then a gradual Decline from one degree to another, until we are even brought to deny the Reality of that Religion & turn Deists. The Christian Religion holds forth Rewards & Punishments—eternal Happiness or Misery—on the purest Principles for the good ordering of Society while here, & our eternal Welfare hereafter. Relinquish the system of revealed Religion, then, on what foundation can you build your hopes of Futurity? The Answer is plainly, On none—or on a State of uncertainty. Miserable state—to be lost in Doubt & Difficulties in a matter that should so greatly concern us. But perhaps some may say, 'Reason is a sufficient guide.' But six thousand years should convince us that, unaided by Divine Revelation, Reason has run into every extreme, every folly, every wickedness. Has not Reason prompted the world in different ages to worship men, beasts, stocks, stones, & even to sacrifice their children to appease a senseless Deity & quiet their Consciences? It may be said that this was not consistent with Reason—it was madness, folly & stupidity. But why do we say so? Because Divine Revelation hath enlightened us: and even Infidels & unbelievers are benefitted by the rational Truths contained in the Holy Scriptures."

Washington, Feb. 26th, 1802.

" . . . . From what I am now going to write, you will doubtless think that I make Absorbents a grand Catholicon in Medicine. If you did, it would be nearly true. Since I have been here, I have directed their use in a variety of cases, & they have never disappointed my expectations. The Patients have been relieved, & if they laboured under a Fever, the fever, after the use of Absorbents, was of short duration; & the Effect produced is founded on the most rational Principles."

Here are extracts from two letters written in Cecil County, in September, 1799, in which, although Æsculapius occasionally flits before us, he is soon fain to hide his diminished head amid the distracting hubbub of war and politics. Could they now be read by the Presbytery which pronounced him "utterly incapable of expressing his ideas upon any subject," it is not impossible that that venerable body, while they might not see in the letters anything to cause them to regret his absence from the ministry, might be disposed to assign some other reason for excluding him therefrom.

" . . . . The news tells us Republicanism is expiring. This comes from the hotbed of Royalty. I am sure, if I admit one fourth of what they relate, I should have a Right to claim by Act of Supererogation. I believe it is right the French should be drubbed. I do not mean finally, but as a chastisement for their many errors & cruelties. [This refers, of course, to the excesses of the French Revolution.] They have been as despotic as the Tyrants they have opposed, & royal Gold has showered down on numbers of them, that they might betray, or at least do acts unworthy of true Republicans. I believe that the King of France was the tenth Horn of the Beast—if so, it was the first that was to be destroyed. Others are also to be destroyed. . . . Then will the Beast & Kings & Emperors fall together into the Bottomless Pit—that is, a State of Neglect—degraded, despised, & at last forgotten."

It is rather amusing that one who, on all occasions, was utterly fearless in expressing his political opinions, should close his letter in this abruptly subdued tone: "Although you may speak of Politics with your Friends, I think you should be cautious that you offend none—no, not a little one."

In the other letter, of date a week later, he writes:

" . . . . When I wrote you last, I stated, that from the Head of Tide upwards, the bilious Fever was general, but that it did not extend far from the River. I can now say it has gone up the Creeks & even the Branches that empty therein. It is like the murderous Suwarrow, who goes where he is not wanted & destroys without mercy; but it is unlike him in this particular—it spares neither Aristocrat nor Democrat, neither Republican nor Monarchist. The Friend to America & the Friend to Britain are all involved in the common fate of the Country.

"What do the dear, dear Friends of Britain think of the Condemnations at New Providence & Jamaica? I trust it will become an Emetic—that they may emit their Monarchy & their Aristocratic Principles. . . . Will America tamely say that the French are the only Pirates, Murderers, Plunderers, Floggers in the World, when, in Nassau, there has been condemned of American Property in the Month of August to the amount of 293,000 Dollars? Will not this open the Eyes of Americans? Why was it done? Because the President has dared to appoint Envoys to treat with France?

In haste, I am," &c.

A sketch of him, which I have not seen, is to be found in Lanman's "Biographical Dictionary of the American Congress." In 1826 Dr. Revere, contemplating the publication of his "Biography of Eminent Physicians of America," wrote to one of Dr. Archer's sons for facts in his career. The following is an extract from a fragmentary sketch prepared in compliance with the above request, but never sent, being afterwards found among the son's papers:

"Dr. John Archer proved himself an able physician during an arduous practice of about half a century. He was successful in many of the important operations in surgery; and as an accoucheur, for judgment and dexterity, was not surpassed by any who had gone before him in the medical world." . . .

In "Hooper's Dictionary, edited by Samuel Ackerly, M. D.," may be seen the following:

"Archer, John, M. D., of the State of Maryland: a celebrated practitioner of medicine. Many contributions of his on various subjects of medical science are to be found in the New York *Medical Repository*. He was the first to introduce seneka snake-root (*polygala senega*) as a remedy in croup. He died in 1814."

* Md. Medical Journal, November, 1889.

The date of his death here recorded is, however, incorrect. It should be 1810. His degree, as given above, is also erroneous; it should be M. B. He was "Doctor" only by courtesy,—having never applied for the second degree. The institution in the first year of its existence adopted a rule that two degrees, M. B. and M. D., should be conferred with three years intervening. In 1792 this rule was discontinued and only the degree of M. D. was conferred. The official catalogue states that very few applied for the Doctor's degree during the early years of the college.

As regards his contributions to the *Medical Repository*, referred to by Dr. Ackerly, I have seen only two of them, describing cases which occurred in his own practice. One was that of a white woman who gave birth to twins—one white, the other black. She was the wife of a toll-gate keeper on the turnpike leading eastward from Baltimore. She confessed that after her husband had left her bed early in the morning, a negro entered her room before she had risen, with whom she had connection. The other case was that of a man whose stomach was cut open by a cobbler with a shoe-knife—the cornbread and cabbage which he had recently eaten rolling out upon the floor. The cobbler sent at once for Dr. Archer, but, being terribly frightened by his own act, sewed up the wound with a wax-end. The doctor let it remain as he found it, and the patient recovered.

His love-letters, written while pursuing his medical studies in Philadelphia, though silly enough in their exuberant endearments, are not a whit more so than those of the average man on such inevitable occasions. Fortunately, he attempts *poetry*—the *sine qua non* of the infatuated lover—but once; and the quality thereof shows unmistakably that he knew infinitely more of Medicine than of the Muses.

In October, 1766, while pursuing his studies, he came on to his native county and married the lady upon whom these endearing terms had been lavished. She was a daughter of Thomas Harris, of Pennsylvania, who had removed to Maryland. He was a member of the family that founded Harrisburg. Among his descendants of the present generation is the illustrious astronomer, Prof. Simon Newcomb. Thomas Harris, in his old days, returned to Pennsylvania and died amongst his kin in Tuscarora Valley, in 1801, over one hundred years of age—*having lived in three centuries.*

Dr. Archer, in his will (dated Sep. 23d, 1808, signed and sealed 29th Dec., 1809, and proved 12th Jan'y, 1811), devised all his estate, real and personal, to his wife Catherine, as trustee for their children (five sons) during her life or widowhood; on her death or marriage, to be divided equally among them. His real estate consisted of about 700 acres of land in one body. He directs, that as there are many persons indebted to him as a physician—many of whom cannot pay without distressing them—"my sons, who are my executors, are directed to make the following entry in cases of such as they think are unable to pay: 'Forgiven by order of the Testator.'" Accounts to the amount of several thousand dollars are so credited in such of his ledgers as are still extant. His male slaves are to be free at thirty years of age, and the females at twenty-five.

Numerous anecdotes have been handed down, which will serve to illustrate some of the more salient points of his character.

A neighbor, who was widely known to be more ambitious of fine display than of satisfying the just demands of his creditors, undertook once (and only once), to rally the doctor on the mean appearance of his badly-groomed and awkwardly-gaited Rosinante,—and, to say truth, he was not over-nice in his selections of horseflesh. "Every hair on this horse is paid for," was the gruff, though well-merited, rebuke.

At a mixed political gathering, he got into a dispute with the sheriff of the county on some exciting party issue. The latter, finding himself worsted in argument, suddenly changed his tactics and came down upon the doctor with brute force, whereupon the assaulted party hurled the pugnacious dignitary to the ground, and was pounding him according to his idea of justice—so that the singular spectacle was presented of one man breaking the peace, whose peculiar duty it was to preserve it, and another inflicting wounds, who had made the art of healing them his lifelong study. Mr. Sheriff, however, soon cried, "Enough!" "Do you pretend to know the dose better than the Doctor, you rascal?" was the uncompromising reply; and it was not until after an additional cuff or two that the restraints put upon the sheriffalty were removed.

Soon after being placed upon the Committee of Observation, in 1775, he met in the public road, on horseback, an influential Tory of his acquaintance, who accosted him in a very excited and insolent manner, when the following colloquy took place:

Tory.—Well, sir, I understand you are part of what is called a Committee of Observation?

Doctor.—I am, sir.

Tory.—And pray, sir, what's the purpose of the d——d thing?

Doctor.—To keep an eye on such scoundrels as you; and, if necessary, thrash them.

The Tory, a powerful man, now leaped from his horse and advanced, as if eager for the fray; but finding the doctor was operating on a corresponding line with characteristic energy, he remounted without loss of time and rode off.

He was wont, when coming upon a party engaged in long-bullet rolling—then much in vogue—to dismount and take part—with the invariable result of beating them all.

Occasionally, when nearly worn out by professional duties, he would steal off to some hospitable home, where he was sure of a welcome, and remain until rested,—not even telling his wife of his hiding-place. A favorite resort of the kind was the home of Mr. Philip Thomas, on Mt. Ararat in Cecil county. This gentleman, (at one time, I believe, a member of of Congress) whose family he attended, was always glad to have him as his guest, and was wont, when the doctor signified his intention of leaving, to place in his way several interesting novels—knowing his weakness for that class of literature. The invariable result was that the guest tarried until he had devoured their contents. This he did eagerly, but in a rather peculiar way—always beginning at the end and reading the events backward.

In his Ledger "I" is:

"Philip Thomas, Esq., Dr.

1797. Nov. 21st. To inoculating twelve of your Negroes, £9.
Nov. 27th. Ad inscrend: Infect: variolæ in Filios (5) et Africanos (32)
To staying with your Family (when inoculated) by your particular request, three weeks - - - - - £29.15"

The doctor's good wife, naturally enough, resented to some extent these prolonged periods of absence in unknown parts. On one occasion, when a stranger appeared at "Medical Hall," and inquired if Dr. Archer lived there, she sarcastically replied: "A man of that name gets his washing done here."

On returning, after one of those prolonged hidings, and entering the office, he found no one there; but on the study table was a pack of cards. Though card-playing was decidedly against the rules, he simply wrote on one of them, in his unmistakable chirography, "This is neither Van Swieten, Boerhaave, nor Cullen." No "devil pictures" were ever afterward seen, at least by him, in that office.

Beneath his manly character and strong intellect ran a vein of superstition, as the following family tradition will show:

About the year 1777 he dreamed, for several nights in succession, that the house in which he was then living—his ancestral home—was struck by lightning and burned to the ground. He forthwith built a house on a distant part of the farm, selecting a very low situation, doubtless to diminish the risk from lightning, and moved into it with his family. He never afterwards would allow the older house to be occupied, although it was commodious and in good repair. The dream was never fulfilled; and it was but a few years ago that the last vestiges of the abandoned edifice disappeared by slow decay. The home to which he removed is still in possession of a branch of the family and retains the name which he so appropriately gave it.

In person Dr. Archer was considerably above the medium height, possessing great bodily strength, and was endowed with a large share of both moral and physical courage. His mind was of the combative order; and although a throat disease had sadly broken his voice—perverting it into a loud, gruff whisper at its best, for the remainder of his days, and totally unfitting him for public speaking—he did not allow the affliction to exclude him entirely from the humbler field of personal controversy. With a vigorous intellect and a good education, he entered zealously the political arena, then in a state of excitement far surpassing that of our own day. Though unflinchingly earnest in the support of his party, he was too independent to degenerate at any time into the demagogue or place-seeker—too honest to be led by public opinion or to allow ambition to swerve him from his convictions of right—one of those bold, self-reliant natures, who, notwithstanding they possess infinitely more of the *fortiter in re* than of the *suaviter in modo*, exercise over their fellow men great influence, being admired for their strength of character and honored for their incorruptible integrity.

Had he applied himself exclusively to his profession, and especially had he been a more frequent wielder of the pen, he would doubtless have left his impress on the medical literature of the country. But being particularly averse to the mechanical part of writing, and being not of those who "seek the bubble reputation even in the" (mortar's) "mouth," his fame as a physician must depend mainly on a few desultory pages hastily thrown off amid the distracting hubbub of war and politics. While the effect of this will be to blend with the image of the skillful physician that of the stern old tyrant-hater, it must impart to his memory a dash of that interest which will ever, it is to be hoped, cling around the names of the prominent participants in our war for liberty.

Dr. Archer had ten children, four of whom died in infancy. Of the six survivors—all sons—five selected medicine as their profession and studied under their father. The youngest of these five, George Washington, died while pursuing his studies. The other four, Thomas, Robert Harris, John and James—named in the order of age—completed their studies at the University of Pennsylvania and practiced their profession. James removed to Mississippi, where he married and died while still a young man, leaving no child that reached maturity. The remaining son—the youngest of all—Stevenson, studied law and became Chief Justice of Maryland, member of Congress, and, by President Madison's appointment, in 1817, Judge of Mississippi Territory, with Gubernatori a powers.

Four of Dr. Archer's sons left numerous descendants, among whom the ancestral proclivity for a roving life seems not yet to have died out. Although many of them still reside in Maryland, a greater number have gone forth to other parts. Some of them live in Virginia and Pennsylvania; several in Texas; and they are becoming quite numerous in Mississippi and Tennessee, with a few in Louisiana and even in the remote State of Washington. Gen. James J. Archer who commanded a brigade under "Stonewall" Jackson in the war between the States, and died in Richmond in 1864, was a grandson of the subject of this sketch; Stevenson Archer, another grandson, was elected to Congress for several terms from the same district which was formerly represented by his father, Judge Archer and his grandfather; and many others of the third and fourth degree of kinship served with distinction in the Southern army.

Dr. Archer sat for his portrait in Baltimore about 1802—the artist being a Mr. Harrison. It was painted for his son, Dr. Thomas Archer. Dr. Robert H. Archer engaged the artist for a replica, which was at once executed, and some time afterwards a copy was made of this replica by another artist for Dr. John Archer, Jr. They are all, I believe, still in existence. The replica, is now about to be presented to the Medical and Chirurgical Faculty of Maryland. Its original owner always said it was much the best of the three portraits. And he mentioned to me as proof of its striking resemblance to the original, that many years, after his father's death, on seeing it in an unusual place and in a rather dim light, he thought, for a moment, that it was his father himself—or, rather, his apparition. A copy of this replica also hangs in the court-room at Bel Air. It was recently taken by a Washington artist, and is very creditably done.

FEMALE POISONERS—ANCIENT AND MODERN.*

By Charles C. Bombaugh, M. D., *Baltimore, Md.*

One of the commentators on the works of the ancient Greek writers, says: "Among the Greeks, women appear to have been most addicted to criminal poisoning, as we learn from various passages in ancient authors." The author most frequently quoted is Antiphon, whose discourses on judicial procedure in Athens in criminal prosecutions, which appeared about four hundred and thirty or forty years B. C., are still preserved. Dr. Witthaus, the toxicologist, in repeating this observation, supplements it with an assumption which may or may not be warrantable. He says: "Women appear to have been most addicted to the crime of poisoning in the Grecian period, *as they are at the present time.*" A repetition may also be noted in Dr. Smith's Dictionary of Antiquities, under the term *Veneficium*, the crime of poisoning. Referring to its frequent mention in Roman history, Smith says: "Women were most addicted to it."

This crime has furnished a theme for novelists and dramatists all the way from the Poison Maid or Bisha-Kanya of India in the Hindu story of the Two Kings; in the *Secretum Secretorum* of Aristotle (XXVIII); and in the *Gesta Romanorum* (XI), to Nathaniel Hawthorne's story of Rappacini's Daughter. Our modern fiction writers, however, generally select their culprits from the male sex, as for example, Charles Dickens in his "Hunted Down," and Charles Reade in "Put Yourself in His Place." Frequent references in Shakspeare's dramatic works, such as the poisoning of Regan, daughter of King Lear, by her sister Goneril, or the removal of Leonine by Cleon's wife in Pericles, show that this, as all else in human character and conduct, could not escape the grasp of the master spirit. He makes Richard II say:

> "Let us sit upon the ground,
> And tell sad stories of the death of kings:—
> How some have been deposed, some slain in war;
> Some poisoned by their wives, some sleeping, killed;
> All murdered."

In Cymbeline, the king's physician, in announcing the death of the queen, surprises and startles the monarch with the revelation of her fiendish purpose to destroy both him and his daughter by a former queen, in order to clear the way for her ambitious projects:—

> "Your daughter, whom she bore in hand to love
> With such integrity, she did confess
> Was as a scorpion to her sight; whose life,
> But that her flight prevented it, she had
> Ta'en off by poison.
> * * * * *
> "More, sir, and worse, she did confess she had
> For you a mortal mineral, which, being took,
> Should by the minute feed on life, and lingering,
> By inches waste you: In which time she purposed
> By watching, weeping, tendance, kissing, to
> O'ercome you with her show," etc.

Sanskrit medical writings, which date back several hundred years before Christ, testify that the Hindus of that early period were familiar with poisons—animal, vegetable and mineral—together with their antidotes. Passages like the following show that criminal poisoning was guarded against:

"It is necessary for the practitioner to have knowledge of the symptoms of the different poisons and their antidotes, as the enemies of the Raja (sovereign)—bad women and ungrateful servants—sometimes mix poison with food."

To various warnings which follow is added the precaution, "Food which is suspected should be first given to certain animals, and if they die, it is to be avoided."

There is abundant evidence that the Persians and Egyptians, as well as the Hindus, were familiar with poisonous substances, such as the venom of serpents, the hydrocyanic acid of the peach kernel, mineral corrosives or irritants, and vegetable narcotics. In the Grecian mythology there is occasional reference to the removal of inconvenient husbands by goddesses who are familiar with the deadly properties of aconite. The manner in which Ulysses neutralized the enchantments of Circe, as related in the Odyssey, shows that attention was given at an early period to the application of antidotes. Homer also tells us of the voyage of Ulysses to Ephyra,

> "to learn the direful art
> To taint with deadly drugs the barbed dart;"

and Ovid relates that the arrows of Hercules were tipped with the venom of serpents, differing in that respect from the modern South American arrow poison, curare, which is a vegetable extract. Poisoned arrows are referred to in the sixth chapter of Job, but there is no reference either in the Old or the New Testament to the use of poison for taking away life.

Of the poisons used in Greece in the historical period, and mentioned by Nicander, the favorite appears to have been hemlock. Whether it was the conium maculatum, or the cicuta virosa or aquatica, is a matter of controversy. Haller contends that the water-hemlock was the conium of the Greeks. It may be noted, however, that Pliny says that the generic term Cicuta was not indicative of a particular family of plants, but of vegetable poisons in general.

For the first circumstantial report of an instance of the class under consideration, we must go back to Antiphon, who, as already noted, lived more than twenty-three centuries ago. In one of his discourses he gives a short speech, entitled "Against a Stepmother, on a Charge of Poisoning." It treats of a case which was brought before the famous court known as the Areopagos. The speaker, a young man, is the son of the deceased. He charges his stepmother with having poisoned his father several years before through the instrumentality of a woman who was her dupe. The deceased and a friend, Philoneos, the woman's lover, had been dining together, and she was persuaded to administer a philtre to both, in hope of recovering her lover's affection. Both the men died, and the woman—a slave—was put to death forth-

* Read before the Johns Hopkins Historical Club, Dec. 12, 1898.

with. The accuser now asks that the real criminal—the true Clytemnestra of this tragedy—shall suffer punishment.

About a century later, the most prominent as well as the most remorseless of the Greek poisoners was Olympias, the wife of Philip of Macedon and mother of Alexander the Great. This restless intrigante compassed the death of Aridæus, a natural son of Philip, his wife Eurydice, Nicanor, and many of the leading men of Macedonia who were inimical to her interests. To those who were imprisoned she allowed the choice between a sword, a rope, and a cup of hemlock; for others there was only the quieting effect of the potion that ended the career of Socrates.

Roman history abounds with cases. While there is reason to believe that in the time of the Empire unwarrantable suspicions were sometimes entertained and false accusations were sometimes brought, we have accounts of numerous murders by poison, the historical proof of which is beyond question. It is also likely that then as now there were many cases in which, in spite of moral certainties and circumstantial evidence, there was failure to convict. In the absence of the facilities afforded by modern scientific methods for the detection of crime, the law officers were correspondingly powerless to intervene, and many criminals escaped with impunity. At the same time there were occasional convictions that were based on mere suspicion. For example, Hostilia, the wife of the consul Calpurnius, accused of poisoning her husband, was thus condemned. Sometimes under the pressure of public clamor and reprobation, offenders were driven to suicide, as in the case of Piso and his wife Plancina, who were charged with poisoning that popular favorite, Germanicus, the nephew of Tiberius and brother of Claudius. Plancina's tutor and accomplice was a notorious poisoner named Martina. More renowned as a professional poisoner of the first century of the Christian era, and held in greater abhorrence was Locusta. Among the victims was Claudius, who was poisoned by order of Agrippina, and Britannicus who was similarly disposed of by order of Nero. This monster loaded Locusta with gifts, and made her teach a selected class her processes, in order that her art might be perpetuated. In this nefarious business, Tacitus, in his Annals, leaves us to infer that slow and wasting poisons were usually employed. He echoes the prevailing belief of his time that skilled poisoners could regulate the effect of their doses with mathematical precision. If so, we shall have to classify their accomplishment among the "lost arts." Our only approach to it is in the latent or dormant condition and eventual outbreak of the specific virus of rabies, yet as the period of incubation runs from a few weeks to several months, we cannot predict the day of impending doom. Theophrastus says that the sorceress used aconite, which makes all the more puzzling his statement that she could regulate the toxic process so as to kill in a month or a year. There is reason to believe that combined with the aconite was the juice of the poppy.

With the secret help of such professionals as Martina and Locusta, the list of ladies connected with imperial and aristocratic families who, from motives of revenge, illicit love, political intrigue, or cupidity, destroyed those who were in their way, is a lengthy one. For the most sensational of wholesale poisonings we must go back to the period of the conquest and the acquisition of Italian territory, three centuries B. C. We learn from Livy that many of the leading men of Rome were carried off with a seizure presenting such similarity of symptoms that it was regarded as the outbreak of a pestilence. It leaked out, however, through information given to the authorities by a slave girl, that these numerous deaths were due to poisons prepared and administered by Roman matrons. Following the clue thus given, about twenty matrons, including Cornelia and Sergia, who belonged to patrician families, were surprised in the act of preparing some drugs over a fire. Upon their strenuous assertion that the preparation was harmless, the magistrates compelled a test of sincerity by drinking it, and thus they all perished. Proceeding upon additional information as to the extent of the mischief, one hundred and seventy Roman matrons were afterward convicted and punished.

From the time of the Lombard invasion to the appearance of the Borgias on the scene of action, in the 15th century, poison was the frequent weapon of the oppressor and the protection or revenge of the oppressed. Lucretia Borgia is said to have shared in the atrocities of her infamous father and brother, though this is questioned by the modern iconoclasts who are bent on reversing history as we have been familiarized with it. During the Renaissance in Italy, poisoning became a fine art; the victims were numbered by thousands, and the female fiend was everywhere in evidence. In the seventeenth century the use of poison as an instrument of secret murder became so common as to warrant a violation of the confessional. In 1659 the priests of Rome informed the Pope, Alexander VII, of the great number of poisonings revealed to them in the confessions of young widows. Investigation led to the discovery of a secret society of women which met at the house of Hieronyma Spara, a fortune-teller, who dispensed an elixir or "acquetta" for the dissolution of unhappy marriages. After a large number of victims had been sacrificed, La Spara's practices were detected through cunning police artifice. She and thirteen of her companions were hanged; others were publicly whipped half-naked through the streets of Rome, and those of the highest rank were banished.

There was a similar society of married women in Naples headed by a Sicilian woman named Tofana, who devised the arsenical solution known as the Aqua Tofana, Acquetta di Napoli, or Aqua di Perugia. It was usually labeled "Manna of St. Nicolas of Bari." Eventually the nature of her transactions was discovered and she was cast into prison. It is said that she was strangled, but whatever her end, it is certain that she confessed, under torture, to instrumentality in six hundred murders by poison, including two Popes, Pius III and Clement IV.

Murrell says that the Aqua Tofana was made by rubbing white arsenic into pork, and collecting the liquid which drained from it during decomposition. To an irritant mineral poison was therefore added, by this vile process, a ptomaine or cadaveric alkaloid possessing properties of the highest degree of toxicity. Be this as it may, there is well-grounded belief that corrosive sublimate and opium were sometimes added to the arsenic.

In other countries there was similar activity in this line. Thierry, the historian of the Norman Conquest, for example, tells us of one queen of the Franks, Fridegonde, in the sixth century, whose life "could be summarized in a chronological table of assassinations by steel or poison"; and of another, Brunhilde, who poisoned her grandson and ten kings or sons of kings.

In Russia, Catherine I, wife of Peter the Great, noted for her scandalous misconduct, is believed to have poisoned her husband; and in France, Francis II and Charles IX were poisoned with the connivance of Catherine de Medici, wife of Henry II, who instigated the massacre of St. Bartholomew, to say nothing of the prompting of the assassination of Henry of Guise and his brother the cardinal. Catherine had in her employ a Milanese named Reni, who served her in the double capacity of perfumer and poisoner. Here, again, the backward swing of the iconoclastic pendulum has challenged the verdict of history, but historic judgment is still firm and impregnable. It is said that the attempted poisoning of Louis VI (Louis le Gros) by his stepmother, in pursuance of her inveterate hatred, was followed to the end of his life by an unnatural pallor. Hence arose the question whether the decoction used was obtained from an herb with properties similar to those alleged of the *Exsangue cuminum*, referred to by the Roman poet, Horace, in one of his Epistles (I. 19).

Of the German criminals of this class, none attracted more profound attention, with one exception, than the devil incarnate known as Nannette Schoenleben. What a travesty this name (beautiful life) is upon her atrocities. On her way to the scaffold she declared that it would have been better for herself as well as for society had she been detected in her first offense and tried and executed for it. "Then," she said, "several lives would have been spared; a vast amount of suffering would have been prevented; and I should not now have had so many crimes to answer for in leaving this world."

The exception noted was a parallel case in Bremen, that of Frau Gottfried. This woman aroused general sympathy by the loss, in the course of a few years, of two husbands, her father, mother, brother and several children, thirteen in all. Their departure was followed by that of members of a family in which she was installed as housekeeper. When she was finally detected in sprinkling grains of a white powder over some meat, the news fell like a thunderbolt upon the community. It was received with stubborn incredulity. Who could believe, said her acquaintances, that one so amiable, so kindly, so pious, so tender and devoted a nurse, so universally respected and esteemed, could be guilty of poisoning her own friends and relatives? She could not, they added, see any one in pain or misery without shedding tears; while the sufferers were writhing in the agonies of death, she called on God to pity them and release them from their anguish. When she was confronted with the evidence of her guilt, the bloodthirsty demon confessed to forty murders during her career, and wrote a history of her life, the details of which are extremely revolting, especially in relation to the murder of her innocent children.

In Spain, the woman who appears to have excited the widest degree of horror and amazement was Donna Maria Mendieta, of Madrid. In conjunction with her paramour, whose name, by the way, was Santiago San Juan, she murdered her husband. Discovery led to arrest and trial. She was one of the most beautiful women in Spain, and belonged to one of its most ancient and honored families. But the judges were inflexible, and both she and her lover were sentenced to death and executed.

In England the most noteworthy case in high life was that of the Countess of Somerset who poisoned Sir Thomas Overbury, in the Tower of London, in 1613, with corrosive sublimate. As Lady Essex, she had procured a divorce from her husband in order to marry Robert Carr, Earl of Somerset. Overbury was in possession of incriminating facts concerning Lady Essex which would have been fatal to her success, and he was put out of the way ten days before the decree of divorce was pronounced. More than two years elapsed before circumstances led to the discovery of her crime. She was found guilty, but was pardoned by James I. This leniency was in marked contrast with the treatment of those who had no friends at Court. A statute of Henry VIII ordered poisoners to be boiled to death, and in accordance therewith it is related that a young woman who had poisoned three families at Smithfield was boiled alive.

In the course of the latter half of the seventeenth century a mania for secret poisoning was developed in France which extended to all classes of society. La Spara and Tofana had fitting types and imitators in Paris in two midwives and fortune-tellers named Lavoison and Lavigoreux. So great was their traffic in poisons, and it may be said, so fashionable, that their houses were thronged with purchasers, both of high and low degree, from Paris and the provinces. The usual motives and incentives were in full play, jealousy, revenge, avarice, court intrigue, political enmity, and removal of all obstacles that stood in the way of iniquitous plans and projects. To suppress and punish this class of offenders, a special tribunal was established in the reign of Louis XIV, known as the "Chambre Ardente." Lavoison and her confederate were condemned and executed in 1680, and their accomplices in various cities of France, to the number of more than one hundred, were burned or beheaded.

Although various noxious solutions were employed by these monsters, the Aqua Tofana appears to have been the favorite. With reference to its results we need not confine ourselves to the annals of medical jurisprudence, for, as has been observed, poets, novelists, and historians have delighted to linger on this chapter of criminal lore, and to paint in vivid colors the tragic scenes which, in Italy, France, and Germany, were enacted by the miscreants who administered the fatal dose with murderous intent.

Of the poisoners of the aristocratic class at that period, none commanded such widespread interest, and none is so well remembered as Marie-Marguerite d'Aubray, la Marquise de Brinvilliers. Here was a woman with every advantage of high birth and position, of large wealth, of influential connections, of singular beauty, of fascinating manners and elegant accomplishments, recklessly throwing all away in the attempt to substitute a scoundrelly lover for a reprobate husband. This lover, Gaudin de Sainte-Croix, who while

incarcerated in the Bastille, in company with the Italian chemist Exili, had learned from him the preparation and application of poisons, so far as then known, became in turn the instructor of the marchioness. This Jezebel in order to test the efficacy of the materials which St. Croix supplied, and to qualify herself for the sure destruction of her father and her two brothers, who antagonized her shameful amour, visited the hospitals, particularly the Hotel Dieu, day after day, in the guise of a sister of charity, to experiment upon helpless invalids. In the course of this diabolical work she often produced effects as mere aggravated symptoms of the maladies she was ostensibly endeavoring to alleviate, and while outwardly gentle, tender, compassionate, and sympathetic, she succeeded in sending a large number to the dead-house without incurring suspicion. St. Croix afterwood lost his life by inhaling deadly fumes in his laboratory; letters compromising the marchioness were found in his cabinet, and she escaped to Liège, but was eventually decoyed from a convent in which she had taken refuge, and brought back to Paris, tortured into confession, and beheaded on the scaffold in the Place de Greve. The best narrative of her romantic career may be found in the admirable historical novel of Albert Smith, better known as an entertaining writer than as an English surgeon.

Coming down to our times, we find in the governing motive a largely diminished ratio of the instigation of the earlier days. Secret poisoning for the removal of people inconveniently in the way of the advancement of wicked ambition, both in domestic and public life, has been displaced to a great extent by the promptings of mercenary rapacity. Vengeance as a mainspring has been transformed into the pecuniary profit that accrues from the death of the victim. In the way of temptation to the flagrant exercise of the avaricious propensity, the life insurance system has innocently widened the range of moral hazard, both in this country and in Europe. But, as we too well know, every organization in the social economy is liable to abuse. How often is the beauty of holiness tarnished by the hypocrites who use the Church as a cloak; how often the holders of fiduciary trusts become defaulters; how frequently the incumbents of official position defraud the government. A system whose outcome proves it to be the best form of organized philanthropy yet devised, cannot be held responsible *per se* for such criminal perversion. That it should so unsex the daughters of Eve, and so metamorphose them into fiends, as the life and accident insurance companies too often have occasion to experience, is a matter for infinite regret.

A complete catalogue for the nineteenth century of the special class of cases under consideration in Europe and America, either under indictment, or subject to the suspicion that is allied to moral certainty, would occupy the entire time and space allotted to this paper. A few instances, taken from the experience of life-insurance companies, will serve the purpose of illustration. That which leads all others in the extent of atrocity is reported from Hodmezoe, Hungary. During the trial, a few months ago, of two Hungarian peasant women, named Jager and Csordas, startling disclosures were followed by confessions of murders numbering several hundred. Their operations were conducted on the plan of the speculative transactions in Pennsylvania and other States, commonly known as graveyard insurance, in which the lives of consumptives, hopeless invalids, paupers and octogenarians were made the subjects of gambling policies without their knowledge or consent, and were hastened to their end by violent measures. In such cases the principle of insurable interest is ignored, and medical certificates are forged. In the cold-blooded procedure of the Hodmezoe conspirators the companies involved were small local beneficial or burial societies, and the amounts at risk were little beyond ordinary funeral expenses. Hence, to make their traffic in human life remunerative, it had to be carried out on a large scale.

Next to this bad eminence or championship was a woman named Van der Linden, in Leyden, Holland. In the latter part of 1883 she was arrested on a charge of having destroyed sixteen lives, most of the victims being members of her own family, including five of her children. She had had their lives insured for her benefit, and received the amount of the policies after their deaths. She confessed her guilt, but her story was so incredible in the boundless wickedness it revealed, that most persons were inclined to reject it in its full extent, even on the assumption of homicidal mania.

In Liverpool, two sisters named Higgins and Flannagan were indicted in 1884 for the murder of four of their relatives, and on trial were convicted and punished. At Deptford, adjacent to Greenwich, Elizabeth Frost and her mother, Mrs. Winters, in 1889, disposed of three cases in similar fashion. Soon afterward Mrs. Winters died, whether purposely poisoned, or whether she committed suicide, is unknown, and, finding her end approaching, made full confession of her guilt. From her dying statement it appears that she preferably employed "white precipitate," but how or why an ignorant woman like her was led to select the ammonium-chloride—to which there is so little recourse—instead of the bichloride of mercury—which is so frequently resorted to—can only be left to conjecture.

With respect to social position, there is a wide gulf between these coarse and vulgar reprobates and such society leaders as the Belgian aristocrat, Madame Marie Therese Joniaux, whose trial at Antwerp, four years ago, for the murder of her sister, brother, and uncle, all insured in her favor, created a profound sensation. She was the daughter of General Ablay, a distinguished cavalry officer; had been brought up in an atmosphere of refinement and cultivated taste; had been twice married to men of superior rank, and had moved among the best social circles of Brussels and Antwerp. But down in the depths of her moral sense she proved to be as depraved, as vicious, as impenitent as the low-born wretches to whom we have referred. Her love of luxury and display and her passion for cards exhausted her fortune, and her nearest relatives were sacrificed to repair it. Yet she was so far above suspicion that it was only the rapidity with which the claims successively matured, and the impetuous and indecent haste with which payment was claimed, that led to her betrayal.

On this side of the Atlantic, the worst case, according to court records, though not the worst in point of fact, is that of Mrs. Sarah J. Robinson, of Somerville, Mass. In 1885, this stony-hearted woman deliberately destroyed the members of

her family, seven in number, one after another, but thanks to the interposition of criminal lawyers and the interference of morbid sentimentality, she has escaped the hangman's rope. In a similar way, another home-destroyer, Mrs. Lizzie Brennan, who killed her husband and two sons at Holyoke, in 1889, evaded justice. With one exception, it should be noted that the entire gang of female poisoners in this country have escaped capital punishment. While this result is usually due to the sympathetic acquittal or the short-sighted disagreement of the juries before whom such cases are tried, there are times when, as in the case of the infamous matricide, Frankie Morris, of Kansas, they are inflexible, and an obviously just and conclusive verdict is neutralized by the subsequent crafty juggling of cunning criminal lawyers. Twenty-five years ago Mrs. Victor, of Ohio, managed her own escape by singing herself with Ophelia-like plaintiveness into the safe shelter of an insane asylum, and thereby into commutation of the death sentence. But that trick cannot be successfully repeated at the present day. The exception noted, to the credit of a Philadelphia jury, was that of Mrs. Sarah Jane Whiteling, who was executed in Moyamensing prison, in 1889, for the murder, by arsenical poisoning of her husband, her daughter aged 9, and her son aged 3, to obtain the paltry amount of their industrial policies, a total of $399.

Aside from sociological considerations, our interest in these cases centers mainly in their relations to medical jurisprudence, medico-legal science, forensic medicine, and especially forensic toxicology, and the present attitude of expert evidence. Questions arise with which we have no concern, and which we leave to the ministers of the law ; for instance, the recent dispute between the authorities of California and the authorities of Delaware as to which should hold for trial the woman Botkin, who is charged with the craftily planned death of Mrs. Dunning and Mrs. Dean, in Wilmington, by poisoned candy transmitted through the mails. That question having been settled, it is now time for the reinforcement of legal chemistry. One of the most perplexing contentions on the part of the defense which the prosecution is compelled to meet is the concordant responsiveness of ptomaines, the alkaloids of putrefaction, to the general reagents for such alkaloids as morphine, strychnine, coniine, atropine, veratrine, etc. In the Sonsogna trial at Cremona, Italy, and in the Lamson trial in London, it was contended that the alleged presence of morphine was mistakenly identified as that of ptomaines, the reaction being the same. The analysts, urged the defense, were not warranted in asserting the existence of a vegetable alkaloid in putrefying material from the affirmative results of the reactions alone. Baumert goes so far as to insist that "in one case the ptomaines in question not only gave various chemical reactions, including the identifying reactions of strychnine, but also possessed the tetanizing action of that alkaloid." In view of such behavior of the spontaneously generated toxic products of putrefaction toward the general reagents, it is not to be wondered at that in the case of Madame Joniaux, at Antwerp, her defenders fell back upon such a convenient theory in spite of the evidence that morphine was found in the intestines of her victims, and that she had repeatedly obtained morphine from Brussels chemists on forged prescriptions.

A case which attracted wide-spread attention was that of Madeline Smith, of Glasgow, who was tried in July, 1857, for the murder of her lover and seducer, Pierre Émile L'Angelier. He sought to crown his perfidious conduct with marriage, but her parents, not knowing of their illicit relations, forced an engagement to marry a man of their choice, Mr. Minnoch. Thereupon the revengeful scoundrel exposed to friends of the family Madeline's piteous letters to him with reference to her *enceinte* condition, and drove her to desperation. The indictment read, "administering arsenic or some other poison in coffee, cocoa, or some other food or drink, in February, 1857." The trial ended with the Scotch verdict, "not proven," to the great relief of the community, everybody being in sympathy with the defendant. In the course of the analytical evidence, several chemico-legal questions were involved, one of the most important of which related to the degree of solubility of arsenic. In the stomach of the deceased the chemists found ninety grains of arsenic either dissolved or suspended, and there was arsenic enough in the intestines to cause violent purging. This, by the way, was seized upon by the defense as consistent with the theory that the deceased died of cholera morbus. But while the crown contended that the arsenic had been administered in coffee or chocolate, the defense claimed that it was impossible that such a quantity could have been taken unconsciously by the deceased in these or any other liquid media. With reference to this view, Witthaus very properly notes that it presupposes that solution is a requisite to secret administration, but while this may be true of a transparent medium, and where the victim is in the possession of his senses, it must not be forgotten that a much larger quantity than could be dissolved may be stirred into a thick and opaque liquid, and taken without producing any effect upon the senses, except possibly a rough taste or gritty sensation. As to grittiness, it may be noted parenthetically, that such crystalline particles could hardly measure up to the standard of the crushed and powdered glass which, in October, a Battle Creek, Michigan, wife of 28 years commingled with the breakfast oatmeal for her husband, a capitalist of 80 years of age. It proved to be quite as potent as the destructives in more common use.

In the case of the American notoriety, Florence Elizabeth Maybrick, tried in Liverpool, in 1889, for the murder of her husband, James Maybrick, it appeared in evidence that the cause of death was gastro-enteritis, which, it was contended, had been induced by an irritant poison. On searching the house, eighty-five grains of arsenic were found. It was proved that James Maybrick was addicted to dosing himself with drugs, that arsenic in minute quantities was one of them, and that not long before his death he had purchased two and a half ounces of it. Even admitting the self-administration of fractional doses, arsenic is not cumulative in the ordinary sense of that term. In discussing the relation between absorption and elimination, it was shown that by the excretory action of the stomach none was left in that organ; that it was chiefly localized in the liver, and minutely disseminated in other organs. Death occurred on the eighth day after the

supposed administration of the arsenic, and this lengthened interval once more brought up the question of possible duration. While the usual period of fatal poisoning is not prolonged beyond twenty-nine hours, there are cases on record in which the end was delayed for twenty-four days. Though the trial, which lasted six days, was largely a battle of experts, it ended in conviction and sentence. As to the motive, the inherent probabilities point less to the amount of insurance on the husband's life than to improper intimacy with another man, and a desire to exchange Mr. Maybrick for Mr. Brierly.

In the Wharton case in this community, in 1871, there was a singular perversion of justice through the quibbling and subterfuge of the experts employed by the defense. It emphasized the conviction that ingenious sophistry may so confuse the judge on the bench, and so confound the jury in the box, that Justice will lend her weight to the wrong balance, and prosecution of guilt will be interpreted as persecution of innocence. Mrs. Eliza G. Wharton was tried at Annapolis on the charge of poisoning her old army friend, General W. S. Ketchum. Several physicians of acknowledged reputation and exalted character testified that Ketchum died from non-natural causes, in other words, from the administration of poison, and three well-known analytical chemists testified that tartar emetic was found in the stomach and viscera, and metallic antimony in the liver. On the other hand, the defense insisted that the death was due to a natural cause, that it was the result of disease, and that the disease was cerebro-spinal meningitis. The witnesses for the State showed that the symptoms and post-mortem appearances were consistent with the theory of poisoning by antimony, and showed, moreover, that the preceding history of the case and the absence of the characteristic lesions precluded the idea of death from cerebro-spinal meningitis. Their position was strengthened and corroborated by the simultaneous attempt to poison Mr. Eugene Van Ness, first with prussic acid, next with strychnia, and finally with tartrated antimony. In both cases the motive was based upon money considerations. The object of the experts for the defense seemed to be not so much to develop scientific truth as to criticise the witnesses for the State, to contend that their testimony was colored by prejudice, and, in one way or another, to impugn their motives. In thrusting forward their audacious assumption, their leader and chief spokesman was Dr. Edward Warren. In his magisterial way he declared that "the case of General Ketchum, from the first pain to the last convulsion, in all its phases, bearings and combinations, illustrates nothing more nor less than a typical example of that form of cerebro-spinal fever to which the name of fulminant has been so aptly given as indicating the suddenness of its invasion, the intensity of its phenomena, the rapidity of its march, and the fatality of its termination." Dr. Warren was supported in his position by several fellow-experts, but it was his own brilliant sophistry that led to disagreement of the jury and escape of the prisoner.

This is neither the time nor place to discuss diversity of opinion respecting questions in dispute in these cases. But a word in passing may be admissible with regard to the interested arguments of experts who are virtually employed and paid as counsel, especially in the line of defense. Common fairness and simple justice demand that both sides of the issue shall be clearly presented, but the Wharton case and similar cases go to show that the expert who has a client to serve, and accepts liberal payment for his services, may discredit this branch of medical practice by constructing a theory or framing an argument so plausible, so ingenious, so persuasive, as to mislead the jury, capture an acquittal, and distort the machinery of justice. The remedy lies in making the position a permanent one in the State, with judicial appointments from the ranks of demonstrated capability and scientific training. We should follow the example of Germany, where, we are told by Casper, "in criminal cases the experts first summoned are exclusively those whom the State, after prior examination of their competency and skill in such particular inquiries, has duly authorized to act for this purpose; while in addition to this, there is organized a tribunal of experts to which the opinions of expert witnesses can be referred." Some of our writers on medical jurisprudence have shown how a similar system can be grafted on our American practice. All that is needed to place our expert evidence upon a higher plane and to bestow upon it a larger measure of respect and confidence is appropriate and readily attainable legislation.

THE HISTORY OF THE MEDICAL DEPARTMENT OF TRANSYLVANIA UNIVERSITY AND ITS FACULTY.*

By William Jephtha Calvert, M. D.

The name Transylvania was first given to that tract of land included between the Ohio, Cumberland and Kentucky rivers. This territory was bought from the Cherokee Indians by Col. Richard Henderson and others for the purpose of establishing a separate and independent government under the sovereignty of Great Britain. The General Assembly of Virginia declared this purchase illegal, and Colonel Henderson was forced to be satisfied with a grant of land on the Ohio at the mouth of the Green River. On December 31, 1776, Kentuckee County, including all of the present State, was established by the General Assembly of Virginia, and three years later Col. Robert Patterson and others began the erection of a fort where Lexington now stands. The newly established county, separated from civilization by the mountains and overrun by a thieving and warlike tribe of Indians, offered to the youth

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no encouragement for education, refinement, or the study of the sciences.

By request, the General Assembly of Virginia, in May, 1780, to counteract these harmful influences, endowed the inhabitants of Kentuckee County with certain lands for educational purposes. This act, donating eight thousand acres of escheated lands to William Fleming and others, as trustees, was the first charter of the school to which, in 1783, was given the name of Transylvania Seminary, and sixteen years later that of Transylvania University. After ten years of religious and political rivalry the seminary was permanently located at Lexington, Ky., with Mr. Moore as its Master. The election of Mr. Toulmin to the Presidency, in 1794, was bitterly opposed by the Presbyterians, who subsequently founded the Kentuckee Academy at Pisgah. Dissatisfaction having already arisen in the new academy, the resignation of Mr. Toulmin from the Presidency of Transylvania Seminary, in 1796, brought about a friendly relationship between the two institutions, which resulted in their union. The new school was called the Transylvania University. The Legislature of Kentucky was afterwards petitioned for a new charter, which was granted December 22, 1798, to take effect January 1, 1799.

The founders proposed to make the new university complete in every branch. The Law and Medical Departments were immediately established, and the libraries and laboratories were equipped as rapidly as possible. The Rev. James Moore was the first Acting-President and Professor of Logic, Metaphysics, Moral Philosophy and Belles-lettres; Rev. James Blythe, Professor of Mathematics, Natural Philosophy and Astronomy; and Rev. Robert Stuart, Professor of Ancient Languages. The Law Department was formally established by the appointment of Mr. George Nicholas to the Chair of Law and Politics. The appointment of Dr. Samuel Brown to the Chair of Chemistry, Anatomy and Surgery; and Dr. Frederick Ridgely to the Chair of Materia Medica, Midwifery and the Practice of Physic, was the beginning of the Medical Department.

From the newspapers of this time we learn that the Medical Society met each week for the reading of original papers and the discussion of current topics.

Dr. Walter Warfield was, in 1801, appointed Professor of Midwifery, and in 1805 the Chair of the Theory and Practice of Medicine was occupied by Rev. James Fishback, M. D.

On account of the small number of students, and for other reasons not recorded, the faculty as a body resigned in 1806. An attempt to reorganize the faculty was made in 1809 when the following professors were appointed: To Anatomy and Surgery, Dr. B. W. Dudley; to Surgery and Obstetrics, Dr. Elisha Warfield; to the Institutes of Medicine, Dr. Joseph Buchanan, and to the Theory and Practice of Medicine, James Overton. Nothing was accomplished by this reorganization. A second attempt was made to reorganize the faculty in 1814, but all of the professors resigned before entering upon their duties. Dr. Dudley,* however, lectured to about fifteen students.

In 1816 a third attempt was made to reorganize the faculty. The following appointments were made: To the Chair of Theory and Practice of Medicine, Dr. James Overton; to Anatomy and Surgery, Dr. B. W. Dudley; to Chemistry, Dr. James Blythe, and to Obstetrics, Dr. W. H. Richardson. In December of the same year Dr. Drake was called as Professor of Materia Medica and Botany. In the fall of 1817 the Medical Faculty was fully organized as a department of the University, and a full course of lectures was delivered to about twenty students, at the end of which the degree of Doctor of Medicine was conferred, for the first time in the West, on John McCollough, of Lexington, Ky.

Dissatisfaction caused the resignation of Drs. Drake and Overton, in 1818, the former going to Cincinnati, Ohio, the latter to Nashville, Tenn. A controversy between Drs. Dudley and Drake, in regard to the resignation of the latter and some matters connected with a post-mortem, resulted in a challenge to mortal combat from Dudley to Drake. The latter declined, but his friend Richardson accepted the challenge. A duel resulted in which Richardson was seriously wounded in the groin, and from which he would have speedily bled to death had it not been for the ready skill of Dudley, who immediately checked the hemorrhage.

While the Medical Department was struggling against adverse circumstances, the Academical Department fared no better. The Trustees had, on several occasions, offered the

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* Benjamin W. Dudley (1785–1870) was born April 12, 1785, in Spottsylvania County, Virginia. In the following year his parents moved to Lexington, Kentucky. His early education was scanty, and of the languages he knew nothing. His medical studies were commenced under Dr. Frederick Ridgely, of Lexington, Ky , and in 1804 he attended lectures in the University of Pennsylvania. Here he met Mr. John Esten Cooke, Daniel Drake and William H. Richardson, all of whom were afterwards his colleagues in Transylvania Medical School. At the close of his second session, in 1806, he received the degree of Doctor of Medicine, and returned home to practice. While in practice he engaged in business, but to what extent is not known. In 1810, he decided to go abroad, where he could study medicine and surgery under the great teachers of his day. Sometime during the year he went to New Orleans on a flat-boat. Here he bought a cargo of flour, with which he sailed to Europe. He sold his flour at Gibraltar and Lisbon and went to Paris. During his four years' sojourn abroad, he spent most of his time in Paris and London, where he took advantage of the opportunities for studying anatomy and surgery. He was one of the leaders in the reorganization of the Transylvania Medical School and taught anatomy and surgery until 1844. From this date, until his retirement in 1850, he was Professor of the Principles and Practice of Surgery.

As an operator he was more cautious than bold, and believed that the preparation of the patient for an operation was essential to its success. He performed lithotomy about two hundred and twenty-five times and operated one hundred times before losing a patient. He operated on all but ten cases brought to him, and lost, in all, five cases. In his practice "a puke and purge, a purge and a puke, were used alike in tuberculous diseases, affections of the hip-joint, spine," etc.

His publications were few and of a practical nature. In his first article he asserted that epilepsy was often caused by pressure on the brain, and could often be relieved by trephining.

After he gave up teaching and practicing, in 1850, he passed the remainder of his life in retirement, and died on June 30, 1870, in his eighty-fifth year.

Presidency of the University to distinguished men; but each had declined the position. The Trustees seeing the bad condition of the University and having lost the confidence of the people, were convinced that political and religious contention must cease and a concerted action be inaugurated. As a result, Dr. Holly, of Boston, was, in 1817, elected President; which position he accepted on June 25th, 1818.

Dr. Holly was a man of unusual ability; his gentle and pleasing manners, his power as a teacher and a speaker, and his high moral character united with his untiring energy were in no small degree responsible for the subsequent success of the University. He entered upon his duties November 17th, 1818.

In the reorganization of the Medical School, Dr. Holly, although not a Doctor of Medicine, took an active part. Through his influence, combined with that of Drs. Dudley and Caldwell, the Medical School soon occupied a prominent position in the University.

Financial embarrassments were removed to some extent by the sale of the public lands donated by the General Assembly of Virginia and by the gifts of private citizens. The libraries were extended, the laboratories enlarged and better equipped, and more spacious lecture-rooms secured. A museum containing pathological specimens, models for anatomy, surgery and obstetrics, was established. Abundant material for anatomy and operative surgery was also supplied.

The following Chairs were represented in the faculty: Dr. Charles Caldwell,* Dean of the Faculty and Professor of the Institutes of Medicine; Dr. B. W. Dudley, Professor of Anatomy and Surgery; Dr. Samuel Brown, Professor of the Theory and Practice of Medicine; Dr. William H. Richardson, Professor of Obstetrics; Dr. James Blythe, Professor of Chemistry, and Constantine F. Rafinesque, Professor of Medical Botany.

In the reorganization of the Transylvania University, the following is the record of the first Faculty Meeting:

"*First Session*, 1819-20, *Nov. 8th*, 1819. The Faculty convened, present—Benjamin W. Dudley, Charles Caldwell, Samuel Brown, William H. Richardson and James Blythe.

"Charles Caldwell, M. D., was unanimously elected Dean, and requested to prepare and deliver, in behalf of the Faculty at the time of their induction into office, an inaugural address.

"Their request was complied with on the 18th of the same month and the address printed at the unanimous request of the Faculty and the Board of Trustees separately expressed.

"[Signed] C. Caldwell,
Dean M. F. T. U.

By W. H. Richardson."

Shortly afterwards we find in the records the following rules to govern the proceedings of the Faculty of Medicine:

"1. Any physician of reputation who shall have been engaged in the practice of his profession for the term of four years, then attended one entire course of lectures in this institution, shall be entitled to present himself as a candidate for the Degree of Doctor of Medicine.

"2. All candidates for said degree must, by the first day of February in every year, signify to the Dean of the Faculty, in writing, their intention to present themselves for examination, specifying at the same time the subject on which they propose to write.

"3. Each candidate, before receiving his diploma, shall satisfactorily sustain an examination before the Medical Faculty alone, and another in the presence of the Trustees and the President of the University. He shall, moreover, write and defend in public (in the chapel of the University or such other place as may be hereafter directed) a dissertation in the Latin, French or English language, pay to the librarian (of the Medical Faculty) the sum of five dollars and the cost of the diploma, which he shall receive. The fee for graduation shall be twenty-five dollars.

"4. Each candidate must be twenty-one years of age, and unless he shall, as above specified, have engaged in practice four years, must have attended two full courses of medical lectures, one of them at least in this University, and the other in some respectable chartered school of medicine, governed by the same laws in granting diplomas with this.

"Thesis must be not less than twelve nor more than forty pages, uniform paper, style and everything considered."

The first session opened with thirty-four students. In the spring of 1820 four students received their degrees, and honorary degrees were conferred upon three. The number of students rapidly increased, reaching in 1826 two hundred and eighty-one. This was the largest number recorded for one session. The number of graduates, however, increased until 1835, when eighty-three degrees were conferred. The total number of students enrolled in the Medical School during the forty years of its existence is four thousand three hundred and fifty-eight; the number of graduates one thousand eight hundred and thirty-three; and forty-four honorary degrees were conferred.

The library of Transylvania University was founded in

*Charles Caldwell (1772–1853) was born in Caswell county, N. C., in 1772. When fourteen he had mastered the Ancient Languages and in the following year took charge of the Snow Creek Seminary. In 1792 he entered the University of Pennsylvania, where he soon gained a reputation as a student. His translation of Blumenbach, in 1795, was the beginning of his literary career. In 1803 he instituted the first clinical lectures in the Philadelphia Alms House, now Blockly Hospital, and was appointed Professor of Geology and Natural History in the University of Pennsylvania, in 1816. In Philadelphia his eloquence gained for him great popularity both as a public speaker and as a teacher. Dr. Caldwell was called to Transylvania, in 1818, to occupy the Chair of the Institutes of Medicine and Materia Medica, and in 1837 he founded the University of Louisville, in which he taught until 1849, when the Board of Trustees asked for his resignation. Later he was occupied in establishing the University of Nashville, which soon became a rival of the University of Louisville.

He was much given to controversy, and his discussion with his teacher, Dr. Rush, shows his antagonistic character. While suffering from a high fever, he had been caught in a drenching rain, from which he expected to die; but to his great surprise he found that his fever soon left him. He immediately reported the fact to Dr. Rush. In his lectures Dr. Rush referred to the incident without giving Caldwell due credit. This aroused Caldwell's indignation to such an extent that he openly assailed Dr. Rush at the commencement exercises of the University of Pennsylvania. The mutual friendship which had previously existed, was now broken and Dr. Rush refused to sign Caldwell's diploma. Referring to the discussion, in his autobiography, Dr. Caldwell says, "Although victory perched on my brow, it cost me the Chair of Medicine in the University."

He was a great advocate of Phrenology and had the misfortune to outlive his favorite theme. "As a man, he was proud and egotistic; as a student, thorough and diligent; as a writer, clear, and as a physician, seldom consulted." He died in July, 1853, in his eighty-first year.

1784, by the Rev. John Todd, of Virginia. Soon after the establishment of the Medical Department, in 1799, five hundred dollars were appropriated for the further equipment of the library. After the reorganization of the Medical Department in 1818, the library was greatly enlarged and well provided with the standard books and journals of Europe and America.

In 1821, Dr. Caldwell was sent to Europe by the faculty to purchase new books and publications. For this purpose he took with him five thousand dollars appropriated by the Legislature of Kentucky, and six thousand dollars appropriated by the city of Lexington.

In the Transylvania Medical Journal for 1828, we find that the library contained three thousand volumes, comprising all of the rare and standard works of medicine and the associated branches of science, besides many publications of Europe and all of America.

After the reorganization of the faculty in 1837, Dr. Peter was sent to Europe to purchase books, apparatus, etc., and we find the following account rendered on March 25th, 1839: books and plates, six thousand dollars; chemical apparatus, two thousand five hundred dollars; preparations for anatomy and surgery, one thousand five hundred dollars; models for obstetrics, five hundred dollars; specimens for materia medica and therapentics and drawing, five hundred dollars. A total of eleven thousand dollars.

The number of volumes at present in the library is five thousand six hundred and eighty-four; pamphlets and medical journals, seven hundred and fifty-four; bound volumes of theses, one hundred and thirty-eight.

The library is now owned by the Kentucky University located at Lexington, Kentucky.

In 1823, Dr. Daniel Drake,* of Cincinnati, was appointed to the Chair of Materia Medica and Medical Botany. On the resignation of Dr. Brown in 1825, Dr. Drake was transferred to the Chair of the Theory and Practice of Medicine, which position he resigned in 1827. Dr. Short was appointed to the vacant Chair of Materia Medica and Botany in 1825, and Dr. Cooke to that of the Theory and Practice of Medicine in 1827.

The following extract is taken from the minutes of a faculty meeting, on February 27th, 1826: "On motion it was resolved to examine six candidates daily, four in the forenoon, beginning at ten o'clock, and two at night, beginning at seven o'clock." All the Professors were present. Examinations were held on Monday, Tuesday, Wednesday, Thursday, Friday and Saturday. An examination was held before the Board of Trustees, March 11th, 1826, beginning at nine o'clock, and concluding at noon. The commencement exercises were held at three o'clock of the same day.

The resignation of Dr. Holly, in 1826, which was brought about by religious contention and the publication of anonymous letters, was a heavy blow to the Academical Department of Transylvania. This department soon sank into insignificance and excepting a few successful sessions in the forties, was never restored to its former position. The Medical Department was now secure, and the subsequent reputation of Transylvania was largely due to this department.

The following are abstracts from the minutes of the faculty meetings:

"Regulations for the Dissecting Room.—The Demonstrator of Anatomy shall be chosen by the Faculty and shall furnish all the material, keep order, clean the room, preserve morbid growths and keep the dissecting room open from six to ten P. M."

"Whereas it has come to the knowledge of the Faculty that John Mason Marble of Tenn., a graduate of the last Medical Commencement, did copy the thesis of a former graduate and present it as his own production, which was received as such by the Faculty, therefore, be it resolved, that the said J. M. Marble be requested to attend another full course of lectures at the coming session and present another thesis of his own composition to the examination of the Faculty, and that the Dean be instructed to transmit a copy of this resolution with the determination of the Faculty in case it is not complied with, to the said Marble."

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* Daniel Drake (1785–1852) was born at Plainfield, Essex county, New Jersey, October 20th, 1785. His only inheritance was industry, temperance and piety. In early life he attended school during the winter months, generally from November to March, and the remaining part of the year worked on his father's farm.

Young Drake in his sixteenth year was sent to Cincinnati to study medicine under Dr. Goforth. He was to study medicine four years and Latin two quarters. His first duties under Dr. Goforth were to read Quincy's Dispensatory and grind quicksilver into mercurial ointment; the latter of which he found, from previous practice on a Kentucky hand-mill, much the easier of the two. At the close of his studies, he formed a partnership with his preceptor; and in 1805 attended his first course of lectures in the University of Pennsylvania.

In 1815 he attended his second course of lectures in the University of Pennsylvania and was graduated in the following spring, receiving many compliments from the faculty.

He returned to Cincinnati in 1816, and immediately acquired a profitable practice. During the year he was called to the Chair of Materia Medica in the Transylvania Medical School; and in the following year returned to Cincinnati to resume his practice.

In 1819 he founded, at Cincinnati, the Medical College of Ohio, in which he was Professor of Medicine. In the following year he was expelled from the faculty, he himself being the presiding officer on the occasion of his expulsion.

He again occupied the Chair of Materia Medica in the Transylvania University in the autumn of 1823; and in 1825 was transferred to the Chair of Medicine, which position he held for two years. In 1830, he was called to the Chair of Medicine in Jefferson College, of Philadelphia, where his eloquence and winning and attractive manners soon gained for him great popularity.

The Medical Department of the Cincinnati College was organized by him in 1835. He became Professor of Medicine, and Dr. S. D. Gross Professor of Pathological Anatomy. He was called to the Chair of Clinical Medicine and Pathological Anatomy in the University of Louisville in 1840, and in 1844 was transferred to the Chair of Medicine, which position he resigned in 1849. During the following year he was Professor of Medicine in the Medical College of Ohio; and in 1850 he was again called to Louisville. Two years later he returned to the Medical College of Ohio, but near the beginning of the session, on November 6th, 1852, death ended his varied and useful career.

As a writer he was interesting, clear and forceful; and was for many years editor of the Western Journal of Medicine and Surgery. During the later years of his life, he wrote a most interesting volume on "The Principal Diseases of the Interior Valley of North America," which was largely the result of his own observations and experience.

Dr. Blythe, in 1830, resigned the Chair of Chemistry and Dr. Lunsford P. Yandell was in the following year appointed to fill the vacancy, with Mr. H. Hubert Eaton, A. M., as his assistant.

In 1835 a summer school was established on the same basis as the winter session. Nine students were enrolled the first year, and sixteen was the largest number during any one year. The summer school was discontinued in 1840 and again reorganized in 1845.

Previous to 1837, the faculty had, on several occasions, discussed the advisability of moving the Medical Department of Transylvania to a larger city. The feelings of the several members of the faculty were not generally known until 1837, when Dr. Caldwell received an invitation from Hon. James Guthrie, of Louisville, Ky., to establish a Medical School in that city. It was first proposed to move the Medical Department of Transylvania to Louisville, but the proposition was soon given up on account of the manifest indignation of the citizens of Lexington and of some members of the faculty. The invitation was accepted by Dr. Caldwell and through his influence Drs. Short, Yandell and Cooke moved to Louisville.

The Faculty of the Medical Department of Transylvania was at once reorganized and consisted of the following members: Dr. B. W. Dudley, Professor of Anatomy and Surgery; Dr. J. M. Bush, Adjunct Professor of Anatomy and Surgery; Dr. James C. Cross, Professor of the Institutes of Medicine and Medical Jurisprudence; Dr. John Eberle, Professor of the Theory and Practice of Medicine; Dr. William H. Richardson, Professor of Obstetrics and the Diseases of Women; Dr. Thomas D. Mitchell, Professor of Materia Medica and Therapeutics, and Dr. Robert Peter, Professor of Chemistry and Pharmacy.

Public interest was awakened and an effort was made to increase the endowment of the Medical Department. In 1838–39, the city of Lexington donated seventy thousand dollars, and a private subscription amounting to thirty-five thousand dollars was given to the Department. The subscription from the professors materially aided in the erection of the new medical hall on the northwest corner of Broadway and Second Streets. The laboratories, libraries and museum were better equipped and the means of instruction greatly improved. The new medical hall was very complete and convenient.

The Chair of the Theory and Practice of Medicine which had been made vacant in 1838 by the death of Dr. Eberle was filled by the election of Dr. Nathan R. Smith,* of Baltimore.

*Nathan R. Smith (1797-1877) was born at Cornish, N. H., May 21st, 1797. At the age of twenty he graduated from Yale, and during the following eighteen months was a tutor in the house of Thomas Turner, of Virginia. At the expiration of this time he returned North and graduated from the Yale Medical School in 1823, taking for his thesis "The Pathological Relations of the Blood."

The following year he began the practice of medicine, in Birmingham, Vermont, and in 1825 was appointed Professor of Surgery and Anatomy in the University of Vermont.

In 1825-26 Dr. Smith visited Philadelphia, where he met Dr. McClellan and others, who were at that time organizing the Jefferson Medical School. Dr. McClellan was favorably impressed with Dr. Smith's professional knowledge and invited him to join their project and occupy the Chair of Anatomy. According to request, Dr. Smith accepted, holding his position two years.

In 1827 he was called to the Chair of Anatomy in the University of Maryland, and in 1829 was transferred to the Chair of Surgery.

On invitation from the Medical Faculty of Transylvania University, Dr. Smith in 1838, accepted the Chair of the Theory and Practice of Medicine made vacant by the death of Dr. Eberle. He held this position three years, when the following letter of resignation was sent to the Dean of the Faculty:

January 7th, 1841.

To R. Peter, Dean of the Medical Faculty of Transylvania University,

My Dear Sir:—It is obviously due to the Faculty of the Medical Department of Transylvania University, whom I have the honor to address through you, that any decision which I may have made in regard to further connection with that department should be announced as soon as made.

I regret to state that circumstances of an imperative nature, and some of them not anticipated, will compel me to resign my chair at the end of the present session. These circumstances are chiefly of a pecuniary character, and cannot but exercise a coercive influence upon one surrounded, as I am, by a young and numerous family, and with my mother's family, at New Haven, consisting of several members, entirely dependent on my exertions.

An unexpected claim, resulting from the delinquency of former Trustees of the University of Maryland, amounting to three thousand dollars, is urged against me. I have no feasible mode of release but by connection with the University of Maryland. It is unnecessary that I should explain particulars.

My residence in Lexington during three winters has satisfied me that practice, having any comparison with that which I enjoy in Baltimore, is not by any one to be hastily obtained here, preoccupied as the field is and limited in extent. The emoluments of my chair, deducting the current expenses of the institution, loss on uncurrent money, etc., would by no means be adequate to my wants, and to continue my connection otherwise than on equal terms with my associates, I should neither desire nor consent to. Indeed, it has been a source of pain to me that circumstances have compelled me to accept thus far the extra considerations named in our contract and always so punctually tendered by you.

Permit me to say that I should not originally have accepted the Chair of Practice on any terms, had there not been some possibility that I should become a permanent occupant of it. I am left, however, free to decide at this time and I am now influenced in my decision chiefly by contingencies which I could not have foreseen.

I assure the Faculty that I am fully sensible that our contract has been an unprofitable one on either part, but I trust they will do me the justice to bear in mind that both last year and the year before, I signified in a letter to one of their body, my willingness to withdraw at any moment that they might be able to make more permanent and satisfactory arrangements.

It will be seen that the circumstances which determine my resignation do not at all involve my personal relations nor my confidence in the stability and future prosperity of the institution. Never have I been connected with an association with whom (*sic*) it could be more agreeable to co-operate. To every member of the Faculty I am incalculably indebted for the flattering estimate which placed me in the chair, and has maintained me in it. The necessity which dissolves my connection with this body will be remembered as one of the most painful of my life, whilst the agreeable intercourse which I have enjoyed with its members and the honor of having occupied a Chair in Transylvania will ever be remembered with the most gratifying associations.

By the influence of the reputation and efficient exertions of the present Faculty and by the munificence of the citizens of Lexington, the Medical Department of Transylvania is now placed upon a foundation which renders its position perfectly secure. Its friends may, without fear of contradiction, pronounce it to be decidedly the best endowed Medical School in America. Its patronage and the emoluments of its Chairs are second to those of but one, and there are none, to be associated with which, I should consider it a higher honor.

Under these circumstances my resignation cannot exercise the least injurious influence upon its prosperity. The chair will immediately command the service of some one whose labors will be more efficient than mine.

You will please, dear Sir, convey to the members of the Faculty assurance of my great respect and affectionate consideration. Yours most truly,

N. R. Smith.

Letter to Dr. Smith from the Faculty.

Dear Sir:—The receipt of your communication informing us that circumstances beyond your control would oblige you to resign the Chair of the Theory and Practice of Medicine in the Medical Department of Transylvania University at the end of the present session, renders some expression of sentiment on our part both just and appropriate.

Permit us, therefore, to assure you that we receive the information of your intended resignation with regret and that nothing would have afforded us more gratification than the certainty of your continuance among us as a fellow-citizen and colleague.

The intercourse which has existed between us for three years during which

Dr. Elisha Bartlett* was elected to fill the Chair of the Theory and Practice of Medicine vacated by the resignation of Dr. Smith. This position he held until 1844, when he also resigned.

The attendance at the Medical School was gradually diminishing, so another attempt was made to place the Medical Department on a better footing. In 1844 the faculty was fully reorganized and the schedule revised. The following subjects were included in the schedule: Materia Medica and Therapeutics, Obstetrics, Chemistry, Anatomy, Surgery, General and Pathological Anatomy and the Theory and Practice of Medicine.

Dr. Lawson, of Cincinnati, Ohio, was called to the Chair of General and Pathological Anatomy and Physiology. Dr. Dudley occupied the Chair of the Principles and Practice of Surgery, and Dr. Bush that of Special and Surgical Anatomy. Four thousand circulars announcing the new reorganization were ordered at Cincinnati.

Dr. L. G. Wilson, of North Carolina, was chosen to fill the chair vacated by Dr. Bartlett.

In 1846 the faculty called for the resignation of Dr. Wilson and the chair was offered to Dr. Bartlett. The death of Dr. Richardson, in 1846, made vacant the Chair of Obstetrics, which was afterwards occupied by Dr. Annan. In 1849, Dr. Annan was transferred to the Chair of the Theory and Practice of Medicine, and Dr. W. M. Bolling, of Montgomery, Ala., was appointed to the Chair of Obstetrics. In 1847 Dr. E. L. Dudley was elected to the chair previously held by Dr. Lawson, and in 1848 Dr. H. M. Skillman was appointed Demonstrator of Anatomy.

The records of the subsequent history of the Medical Department have been either lost or destroyed, excepting the matriculation book, which shows that the number of students gradually decreased from year to year until 1858, when twenty-three students were enrolled. This was the last session.

During the Civil War the Medical Hall was used by the Union forces as a hospital and stable. It was later destroyed by fire. The libraries and apparatus were removed to Morrison Chapel which now belongs to the Kentucky University.

we have been associated, has been of the most harmonious and pleasant character, and the ability with which you have performed the duties of your Chair increase the reluctance with which we give up the expectations of a longer co-operation with you under the auspices of the Transylvania University.

With the most sincere wishes for your continued increase in fame and prosperity, we remain your friends and colleagues,

THE MEDICAL FACULTY OF TRANSYLVANIA UNIVERSITY,
ROBERT PETER, Dean.

On returning to Baltimore Dr. Smith occupied the Chair of Surgery, in the University of Maryland, until 1870, when he retired.

As a surgeon, he was famous; as a citizen, philanthropic and beloved.

His chief works were: "The Surgical Anatomy of the Arteries;" "Fractures of the Lower Extremity." He invented an anterior splint to be used in fractures of the lower extremity, and a lithotome.

His death occurred July 3, 1877.

* Elisha Bartlett (1804-1855), was born at Smithfield, Rhode Island, October 6, 1804. His early education was received from the best seminaries in the places where he occasionally resided. His professional education was of the same varied nature. Having studied at Uxbridge, Worcester, Burton, Providence, he received his degree from Brown University in 1826. "His varied education made him familiar with, and attractive in, all social circles, easy and graceful in his manners, and universally popular."

After graduating he repaired to Paris for the further study of medicine. Leaving Paris after a year's profitable study, he journeyed into Italy before returning to America.

His first residence in America, as a physician, was at Lowell, Mass., where he soon enjoyed a lucrative practice. He married in Lowell in 1827, and in 1828 accepted the Chair of Anatomy in the recently established school at Woodstock, Vermont.

He was appointed Professor of Pathological Anatomy in the Berkshire Institute at Pittsfield, Massachusetts, in 1832, and in 1844 the University of Maryland offere l to him the Chair of the Theory and Practice of Medicine. In 1850 he occupied the Chair of the Institutes of Medicine in the University of the City of New York, and on the death of Dr. Beck was called, in 185', as Professor of Materia Medica and Medical Jurisprudence, to the College of Physicians and Surgeons of New York. Owing to his failing health he soon gave up his professorship and retired to Smithfield, Rhode Island, where he died in 1855.

He was, in 1836, chosen the first mayor of Lowell, and, in 1840, was sent as representative to the Legislature of the State of Massachusetts. As a writer, he was clear and interesting; as a speaker, eloquent and attractive.

SKETCH OF JOHN CRAWFORD, M. D.*

BY E. F. CORDELL, M. D.

(*Read before the Johns Hopkins Historical Club, May*, 1899.)

Although now quite forgotten by the profession of this city and State, there is no name in all its annals more honorable or worthy of perpetuation than that of Dr. John Crawford, of Baltimore. His life, character and writings afford abundant material for a biographical sketch of the deepest interest. He was the second son of a clergyman in the north of Ireland, where he was born May 3, 1746. His family was highly respectable but poor. His father was a scholar, a man of talent and piety, who raised his children in the love and fear of God. The seeds thus sown brought forth a rich harvest of virtues in the son, the subject of this memoir. His brother, Adair, achieved eminence in England and is spoken of as "one of the most

* Dr. Quinan, *Med. Annals, sub voce*, has placed a "Rev." after Dr. Crawford's name. The deep religious fervor of the latter, so unusual in a medical writer, may have suggested the idea that he was a clergyman; or, Dr. Quinan may have confounded with him a "Rev. John Crawford," who resided in Baltimore at one time and some of whose writings are extant. There is no justification for the clerical title.

brilliant ornaments of medicine and philosophy" in that country.† John was reared among his family until the age of 17, when he was sent to Trinity College, Dublin, to pursue classical studies. Thence he went to the University of Leyden, which was then in high repute, owing chiefly to the great fame of Boerhaave, and there he received the degree of Doctor of Medicine. He then made two voyages to the East Indies as surgeon in the East India Company's service, receiving on his return the thanks of the Company and a considerable sum of money for his zeal and fidelity. During these voyages he kept a diary, from which very interesting extracts were published in the Edinburgh "*Annals of Medicine.*" About the year 1778 he was married, and shortly after received the appointment of Physician-in-Chief to the Hospital in the Island of Barbadoes. This was a position of great honor, and it might also, in other hands, have proven an avenue to great wealth, for Dr. Crawford had under his control large contracts for supplying the British fleets on the West India station. But with that magnanimity and self-neglect which so often characterize men of lofty character and purpose, he cared but little for wealth and allowed opportunities for acquiring fortune to go, without even a share of their profits, to others. In the year 1780 the island was devastated by a terrible hurricane, and this afforded occasion for the exhibition of his generous and humane disposition. Amidst general ruin his property alone remained intact, and not a single medicine was left upon the island except what was in his possession. He refused to profit by the common distress, but supplied medicines and other aid to those who needed them without stint and without compensation. In 1782 bad health compelled him to return to England. During this voyage his wife died under very distressing circumstances, leaving to him the care of two infant children. Having recovered his health he returned to Barbadoes, but soon after removed to Demerara, where he had been appointed Surgeon-Major to that colony then in the possession of the Dutch. During his residence at Demerara the authorities conferred high honors on him, and he had frequent opportunities for the exhibition of that philanthropy which was his peculiar attribute. His house, his table and his purse were open at all times and to all. Strangers especially profited by his open-handed hospitality. But he did not neglect professional duties and interests. The military hospital with 60 to 80 beds, and absolutely under his control, afforded a wide field for observation and study, and he made a large number of autopsies. An observation which he made at this time was the frequency with which he found abscess in the liver where there had been no symptoms pointing to its existence during life. About the end of 1794 his health again gave way under the influence of bad climate, and he was obliged to return to England. Thence he went over to Holland to settle business affairs with the Dutch government. During his stay in Holland most of his time was spent at Leyden in study and research. Meanwhile Demerara was transferred to the control of the English. Although he was offered by the English government the same position which he had recently held in the colony, in the interest of his children whom he desired to be well educated, and by the solicitations of a brother-in-law who had already crossed the water, he was induced to decline the offer and embark for the United States. He arrived in Baltimore in 1796, the year the city charter was granted, and about the same time Drs. Davidge and Potter settled here. Thenceforth, for seventeen years, Baltimore was the scene of his mature life-work. A man of such a character and acquirements could not long remain obscure in any community. "The unaffected urbanity of his address and manners," says his biographer, "the sweet benevolence of soul, the innate dignity of mind which shone with such animated luster in every lineament of his noble, manly countenance, soon gained him the acquaintance and esteem of all whose respect is valuable of every class of his fellow citizens." A professional career would furnish such a generous nature many opportunities for the exhibition of a humane and unselfish conduct, but such acts form but the ordinary routine of a good physician's life and their existence is only known by their being the necessary accompaniments of such a life. Of Dr. Crawford's public acts we know more. He was a participator, if not a leader, in most of the humanitarian enterprises of his day. The Baltimore General Dispensary, established in 1801, owes its origin directly to him, and he continued an active manager of it until his death. He was also connected with the Hibernian Benevolent Society from the earliest period of its existence and held several offices in it. To his indefatigable exertions, perhaps, more than to those of any other individual, is the State indebted for the establishment of the Penitentiary. He was one of the founders of the Bible Society of Baltimore, an association of Christians of every denomination, designed to promote the spread of the gospel among all men.* He was also one of the directors of the "Baltimore Library," the first institution of the sort in the city. There is extant a lecture delivered by him at the Medical College, in November, 1811; it is entitled, "*Introductory to a Course of Lectures on the Cause, Seat and Cure of Diseases,*" 8vo., pp. 51. In November, 1812, he began another course on Natural History, on Hanover street, continued later on Commerce street. This course was also under the auspices of the college, and was to have been given at the college on Lombard street, but the building was not sufficiently advanced at the time for occupation. The title of the chair which he held from the Regents of the college was "Lecturer on Natural History." He was soon compelled to abandon this course, but the reasons for its discontinuance are not given. Of the lectures which he gave his biographer says: "His compositions were remarkable for

† I find the following notice of Dr. Adair Crawford, in the *Cyclopædia of Biography*, by Parke Godwin, N. Y., 1880: "Physician and Naturalist. Physician to St. Thomas' Hospital and Professor of Chemistry at Woolwich. Author of several chemical works." In his lecture on "The Cause, Seat and Cure of Disease," Dr. John Crawford refers to his brother as "my revered brother . . . who was the first to ascertain by actual experiment that animal heat was derived from the air in respiration, and thus brought to a conclusion the conflicting opinions on that intricate subject."

* He was a director of the "Maryland Society for Promoting Useful Knowledge," founded in 1800.

correct and elegant style, and . . . displayed a soundness of erudition and a depth of research seldom equaled." Dr. Crawford's professional standing and enterprise are also shown by the part he took in the introduction of vaccination in this country. He received a supply of virus from Dr. Ring of London, in the summer of 1800, and was successful in its use.* This was contemporaneous with its use in Cambridge, Massachusetts, by Dr. Waterhouse, to whom the credit is usually given of having been the first to employ it in America.

With such sentiments and such a desire to be useful to his fellow-men, it is not surprising that he drifted into an organization which holds charity to be a supreme virtue and duty. He became connected with the Masonic Order here in 1798. In this he had a wider field for the exercise of that benevolence which was a part and a very necessity of his nature. He rose at once to the highest office in his Lodge and was recognized as a leader among his brethren in the State. In 1801 he became Grand Master, having already presided at most of the meetings of the Grand Lodge during the previous two years. After this he was continuously and unanimously elected to the same office, with the exception of one year when his professional engagements compelled him to decline, to the period of his death in 1813. The charges which he delivered to his brethren in the Grand Lodge have been preserved and they are models of style and of Christian fervor. So highly esteemed were they by the fraternity that in order to diffuse their beneficial influence more widely they were in some instances published and distributed among the order in other States. His numerous Masonic writings, including a work upon Masonry, which he had prepared for publication, were bequeathed by his will to his "beloved friend Nicholas Le Favre, Esq., of Philadelphia, Gentleman." He also wrote many medical articles which are highly interesting and valuable. He was a large contributor to the "Medical and Physical Recorder," 1808–9, edited by Dr. Tobias Watkins, the first medical journal published in Maryland. His medical writings were bequeathed to Dr. William Donaldson, of Baltimore, and have probably been destroyed. Although—and it seems strange—Dr. Crawford did not enjoy the honor of being an incorporator or founder of the Medical and Chirurgical Faculty of Maryland, he held high rank in its early councils, being censor, examiner, orator, and member of the committee appointed to publish its transactions. He was also Chairman of "The Medical Faculty of Baltimore" and as such made a report on the health of the city to the City Council, February 10, 1800. He was Vice-president of the Medical Society of Baltimore and Consulting Physician to the Board of Health and City Hospital. Doctor Crawford died at his residence, corner of Hanover and German Streets, on the morning of the 9th of May, 1813. Of the nature of his illness we are not informed, but it was brief and violent in character. The Grand Lodge was then in session. He attended the meeting on May 4, and delivered an annual address as usual. It is said to have been able and excellent—"the production of his rich imagination, couched in the most affectionate and parental language." At its conclusion he intimated to his brethren his wish to retire from office and pleaded in excuse for not serving longer his already lengthy services and advanced age. He then withdrew, giving the Tyler an affectionate shake of the hand as he passed through the adjoining room, and remarking that the door which had just closed upon him would never again be opened for his reception. Hardly had he left the lodge room before the members, by spontaneous act, gave him a unanimous vote of continuance. His presentiment came true. Owing to the apprehension consequent upon the approach of the British, the Grand Lodge did not meet again until the 9th of the month. Meanwhile, on the very next day after his attendance, he was attacked with the fatal illness which terminated his life in less than four days. On the 10th of May the Grand Lodge was convened and followed his remains in sad procession to the Presbyterian graveyard, corner Fayette and Greene Streets, where they were duly interred. In the following June a monument of sandstone and marble, carved with masonic emblems and containing an inscription conveying the chief facts here stated, was erected in his honor.

Dr. Crawford left one child, a daughter, who married Mr. Maximilian Godefroy, an architect and the designer of many of the public buildings of this city. It is not known whether she had any children. Dr. Crawford's library was purchased from his widow by the Regents of the University of Maryland and formed the nucleus of the library of that institution now known, from the larger bequest of another physician, as the "Brune Collection."

The character of Dr. Crawford seems to have excited the admiration and reverence of every one who came in contact with him. His urbanity, his unselfishness, his tireless charity, his forgetfulness of injury, his genuine human sympathy, his earnest Christian piety and his social virtues, made him a model for imitation. His scientific and professional attainments and position were conspicuous and freely acknowledged. His time, his labors, his cares and his fortune were devoted to the cause of suffering humanity. One writer says of him: "Since the days of the celebrated Howard that man has not appeared on the stage of life whose character so nearly resembled that celebrated philanthropist as Dr. Crawford." Many remarked his strong resemblance in face and form to Washington. Nor did this resemblance, which appears in his picture, stop at the exterior; there was also a close identity of sentiment, motive and character. There can be little doubt that upon a larger field of action, Dr. Crawford would have proven with equal certainty that he possessed the same elements of greatness; for greatness is not insured by the mere possession of certain qualities of mind and heart but requires an opportunity also for its exhibition.

Dr. Quinan (Medical Annals of Baltimore. 8vo. Baltimore, 1884) gives the following list of writings of Dr. Crawford:

Thesis (title unknown); Journal of a Voyage to Bombay and Bengal as Surgeon in the Employ of the East India Company, 1772; Observations on Native Camphor, Medical Communications. Edinburgh. Vol. 8, p. 253, 1793; On a Disease of the Liver hitherto little known. London. 8vo., 1776 (?); Report,

* *Ring on Cox-pox*, 1801, p. 496. (quoted by Quinan).

as Chairman of Medical Faculty of Baltimore, to City Council on Health of the City, February 10, 1800; Address at Grand Convention of Frec Masons of the State of Maryland. Dobbin & Co., Baltimore, 1802. 8vo., pp. 48; On the Sanicula. Baltimore Medical and Physical Recorder, Vol. 1, 1809; Hepatic Cases, Same, 1809; Case of Ascites, Same, 1809; On Seats and Causes of Disease, Same, 1809; A Lecture Introductory to a Course of Lectures on the Causes and Seats of Disease, etc. E. J. Coale, Baltimore, 1811. 12mo., pp. 51; Four Letters on the Treatment of Yellow Fever. Federal Gazette, September, 1802. To these I would add: Remarks on Quarantines. Baltimore Observer, Vols. 1 and 2, 1806–7. Dr. Crawford also delivered one of the Biennial Orations before the Medical and Chirurgical Faculty in 1805, but I am not aware that it was published.

Of the above I have had access to the Masonic Addresses, the lecture on the Seat, Cause and Cure of Disease, and the Remarks on Quarantines. Several others can be seen in the "Medical and Physical Recorder," 1808–9, edited by Dr. Tobias Watkins, a copy of which is preserved in the Surgeon-General's Library in Washington. I may say, in passing, that some of the purely literary articles in the Baltimore Observer are doubtless by his pen, and I have a strong suspicion that the lady editor of that periodical was his own daughter.

I direct your attention now to Dr. Crawford's writings as they have come under my notice.

A strongly religious tone pervades his works; it has a genuine ring and is altogether free from cant: "There is one course I shall pursue," he says, "which has been strangely neglected by medical writers—never to lose sight of the Creator."* Speaking of the infidelity prevalent among the "Faculty," he says that professional study, being directed to the physical causes and operations of the animal economy, tends to a neglect or undue appreciation of the spiritual side of life. Hence, physicians are disposed to attribute to secondary causes things which can only belong to first; and so, resting there, they lose sight of a Divine cause. It cannot be that true religion and true philosophy are ever at variance with each other; on the contrary, when rightly understood they mutually and powerfully support each other. Who but the Deity, he asks, could operate the wonders that are continually pressing upon our regards? Attributed to a divine source, wonder is changed into admiration, reverence and devotion! Philosophy can never be brought to perfection unless the mind of the investigator is suitably impressed with the necessity of having his thoughts continually directed to the stupendous Author of all things. It cannot be too frequently or too strongly urged that our success will be precisely in proportion to our discovery of the designs of Him by whom the objects of our inquiry were contrived and executed.

Passing on to the more strictly medical writings—I refer particularly to those on Quarantine and on "The Cause, Seat and Cure of Disease"—in these he discusses principally the origin of disease, and it is his views upon this subject that especially rivet our attention and constitute, as I think, his title to fame. The lecture on "The Cause, Seat and Cure of Disease," besides outlining the course which he proposes giving,† deals almost exclusively with the first of the three subjects named and in the more general way of an introductory lecture. It is in the article, or series of articles, on Quarantine that he enters into the details of the subject and produces his facts. I regret to say that the volume containing the latter was not known to me until two days ago and I have had opportunity for only the most cursory examination of it. The volume in which it is contained (Baltimore Observer, a weekly literary publication, commencing November 29, 1806 and continuing until the end of 1807) of which there seems to be in all our libraries but one copy, is the property of the Maryland Historical Society, and the rules of that body do not allow it to be taken out. It is not catalogued and we only knew casually of its existence. Therefore, I am not able to give such a careful analytical review of it as I would wish. I learn, however, that Dr. Crawford first began to entertain the idea of an animated principle, a contagium vivum, as the cause of disease, about 1790, when he went to reside in Demerara, or Guiana. He saw there, of course, a large number of cases of malarial and yellow fever. At the close of the day when the beams of the sun fell aslant upon the earth he saw myriads of minute insects—at other times invisible—fluttering in the air. He said to himself, "if in the air why not in my air tubes? and why not thus the conveyors of disease?"

All analogy taught that disease and decay were coincident with the presence of minute organisms. Such was the case with the putrefying flesh exposed to the air, such with the decaying fruit, such with the rotting wood, such with the moth-eaten garment, the rusted grain. If the fly lays its eggs to develop later into the crawling worm, why may not minute insects deposit their offspring in our bodies, there to develop and ravage the tissues? And he declared that this was a law of universal application, not more applicable to the lower animals than to man, and embracing the vegetable kingdom as well as the animal.‡ With these views he returns to Leyden; and

* Cause, Seat and Cure of Diseases.

† "I shall first submit to your consideration a succinct account of the diseases of the human body, the causes of which have been made evident to the senses. . . . I shall then proceed to consider the cause of suffering in the animals that are in nearest connection with us, continue my inquiries through all the animal tribes down to the smallest insect as far as the means of information have been within my reach, and finally advert to the leading sources of destruction in the vegetable kingdom. I shall then revert to man, and hope to reflect the light elicited from them on what is obscure in our own species, etc."

‡ "There is a principle which pervades the whole circle of nature of which we should never lose sight; it is that every individual existing is more or less a type of every other, although no two things whatsoever are exactly alike." Balt. Observer, II, 3, July 18, 1807.

Again: (These animalculæ) "do not spare *even ourselves*. They have been traced through all their various operations and changes on every occasion except the last" (*i. e.*, in man). "Here our progress has been arrested, here our efforts have been palsied. There is not yet an individual, whether naturalist or physician, who has traced diseases to this source or viewed them as constituting a part of the general law of nature. We have seen that in Gaubius, in Boerhaave, and much more in Linnæus and his followers, there are

there, while reviewing some Dutch troops just back from a campaign in the marshes, he enunciates it to Professor Brugmans, Professor of Natural History and Botany in the University, and another physician who was present. He learns from them to his surprise that such views were not new. Yet there was no mention of them in any of the works on medicine of the day. He mentions a number which were silent on the subject. He continued this line of investigation. He became more and more convinced of the truth of this view. It was with him not a mere hint—a suggestion, a fancy, a possibility or a probability—but an overmastering conviction and the dominating principle of his life, his thought, his conduct. He seems to have realized its predominating importance, that it furnished at once the solution of a problem which had puzzled the greatest minds of the past and led to the greatest variety and absurdity of opinion. More than this, that it furnished a rational method of treatment. Dr. Crawford was a man of learning and genius, and possessed the true scientific spirit. "I shall studiously avoid . . . offering any opinion," he says, "when I have not an ascertained fact to support it." As a comparative pathologist, I doubt if he had a superior. And whilst others had conceived the theory of a contagium vivum, none urged it with the same absolute conviction of its truth, the same mental certainty, the same mastering prevision as he. I think I cannot be wrong in stating this. Certainly he was far ahead of his day in his views—at least seventy or eighty years. What would such a man have accomplished had he been backed by the resources of such an institution as this? He not only held these views as to the cause, but he carried them to their legitimate conclusion as to prevention and treatment. He insisted upon absolute cleanliness and all those things that go to make a perfect hygiene—pure water, pure air, pure food, proper clothing, proper sewerage, and a regulation of the habits of living, but above all and including all, cleanliness. He insisted also that the sick should be removed from, and the well prevented from going to, infected localities, infested in his view with the morbific but invisible agents of disease. In the treatment of disease, likewise, he employed remedies with a view to their destructive effect upon the pathogenic organisms. What is this but antiseptic treatment? Did he not thus anticipate the modern methods of treatment and take the first step that led to the triumphs of Lister? It is true he used the remedies that were in vogue, but he used them upon a different principle and for a different object from those which other physicians had in view. Nor were the results of these investigations to be judged only by our ability at once to control and influence epidemics. "If no other benefit should result from such an investigation, the satisfaction that must be experienced in at all comprehending the nature of what is to be done, and clearly seeing the course that ought to be pursued, will be a blessed exchange for the confusion and doubt which at present exist."

We need not be surprised to learn that he met with opposition, with ridicule, with incredulity. No doubt he was regarded as a "crank" by his medical associates, for every great reformer who has a new truth to teach has such an experience. It is probably for this reason that he sought to inculcate his views through the medium of a lay journal. There is something extremely pathetic in the conclusion of his lecture on "The Cause, Seat and Cure of Disease," 1811. He expects opposition to his view but is prepared for it, has no disquietude as to the result, and would proceed perseveringly with his investigations, hoping to convince those who were not blinded by prejudice against the truth. He was willing to make any sacrifice to attain this object and to submit to any deprivation. "Our ignorance upon this matter cannot continue always," he prophetically declares, "for it is not beyond the limits of human intelligence." Fortunately, he was supported in his purpose by a mind which did not crave luxuries, but was satisfied with the necessaries of life; his inclinations were all averse to extravagance and the plainest fare was as acceptable to him as the richest viands. Having already advanced far in his 65th year, the charms of life had largely lost their attractions and there was, therefore, no impediment to his continuing in the path which he had followed for nearly twenty years. "The difficulties I have had to encounter," he concludes, "have indeed increased my ardor. As long as health and life remain, I shall deem myself strictly in the performance of my duty whilst so employed and I shall leave the result to that august Being who has made nothing in vain and who often makes use of the humblest instruments to accomplish his all-wise purposes lest presumptuous man should assume to himself the glory which belongeth alone to God." And so within a brief space passed out of this world this good man, this wise physician; and I venture to think you will agree with me that no one who is engaged in the study of pathology, nay, of medicine itself, can afford to be ignorant of his name and work.*

The writer desires to acknowledge his indebtedness for much of the biographical part of this sketch to Schultz's "History of Freemasonry in Maryland," Vol. II, 1885.

discoverable many hints to the same effect; but previous to my attempt, I believe I may assert, there is not one who has seriously endeavored to show that there is equally one law by which every animal without any exception is undeviatingly governed."—*The Cause, Seat and Cure of Disease.*

*Since this paper was written I have re-read Dr. Crawford's papers in the *Observer*, and find that I have represented him correctly. I shall not, therefore, change what I have written.

THE JOHNS HOPKINS HOSPITAL BULLETIN.

The Hospital Bulletin contains announcements of courses of lectures, programmes of clinical and pathological study, details of hospital and dispensary practice, abstracts of papers read and other proceedings of the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly.

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A CASE OF ACUTE SUPPURATIVE CHOLECYSTITIS WITH ISOLATION OF THE BACILLUS TYPHOSUS EIGHTEEN YEARS AFTER AN ATTACK OF TYPHOID FEVER.*

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The following case is considered worthy of report, first, because of the great interest shown in recent years in the questions of cholecystitis and cholelithiasis; and second, because of two interesting features in the case itself, viz., the long period elapsing between a probable typhoid infection and the acute cholecystitis; and again, the peculiar morphological and staining properties of the bacillus isolated.

A German woman, aged 54 years, was admitted to the service of Dr. Kelly on February 3, 1899, seeking treatment for a large abdominal tumor. Her family history was unimportant, except that her father had died at the age of 60 with "yellow jaundice." She had given birth to four children, the oldest now being 32 and the youngest 21 years of age. She gave a history of childhood's diseases, and of particular interest was the history of an attack of "remittent fever" eighteen years ago. She was in bed only two weeks, and then insisted upon getting up, although her illness continued for two months. There was typhoid fever in the neighborhood at this time.

She first noticed enlargement of the abdomen three and one-half years ago, after getting up from a serious illness of six weeks' duration. This illness began suddenly as a severe pain in the right side, radiating down into the right inguinal region. The pain became intermittent in character, the attacks lasting one-half hour or more and leaving the patient nauseated and with abdominal tenderness. She had no vomiting and no jaundice, but suffered from several attacks of diarrhœa.

For two years following this illness the patient was well, though suffering occasionally from slight pains and soreness in the right side. She also observed a small movable mass in the right lower quadrant of the abdomen.

Eighteen months before admission to the hospital her attacks of pain increased in frequency and severity, and often after a paroxysm she could not bear the weight of her clothing. Recently she had been confined to bed for short intervals and had lost weight and strength.

Physical examination revealed the presence of a large cyst springing from the left ovarian region. The right ovary was represented by a hard, movable mass, of the size of a fist, lying high in the lower right abdominal quadrant.

For this condition Dr. Kelly operated on February 6, removing both tubes and ovaries with the ovarian cyst. Numerous adhesions to the intestines and omentum were severed or torn apart, and an adherent appendix was removed.

The period of early convalescence was without special interest, the abdominal wound being found healed on the tenth day.

On the fourteenth day the patient complained of nausea and vomited several times during the afternoon and evening. She had no distension and no particular tenderness. She was more comfortable on the day following, there being no nausea or vomiting. Her temperature reached 100.3° F., and the epigastrium was somewhat sensitive.

At 10 A. M., on the sixteenth day, she suddenly began to complain, as before, of great pain in the epigastrium. Her expression was anxious, and there was profuse perspiration. The temperature was 99° F., and the pulse rate 96. In the epigastrium one could see peristaltic waves from the distended stomach, and at the right costal margin a sensitive tumor which was dull on percussion could be palpated. At 8 P. M. the temperature reached 101° F.

On the seventeenth day her condition became very critical. The pulse rate and temperature, at 4 P. M., were respectively 140 and 103° F. A visible tumor, exquisitely tender, protruded from the costal border in the right hypochondrium, and the gastric distension was even more marked than before. The leucocyte count at 3.30 P. M. was 29,000.

There was some question as to whether we were dealing with a localized abscess, following the removal of the appendix, or with an acute cholecystitis. Her history might well have pointed to repeated gall-stone attacks during the past three and one-half years, although up to and during the operation these attacks of pain had been considered due to localized peritonitides associated with the growing ovarian tumors.

Operation (Dr. Stokes).—Cholecystostomy; evacuation of contents of greatly distended gall-bladder; permanent drainage.

An incision over the tumor to the right of the rectus border revealed a greatly distended and congested gall-bladder. Surrounding this were found numerous fresh adhesions and a sero-fibrinous exudate in the peritoneal cavity. No stones were felt on investigation of the bladder and ducts.

After suturing the bladder to the abdominal wall an incision was made allowing the free escape of a large quantity of straw-colored mucoid fluid. Investigation of the deeper portion of the gall-bladder by the fingers was followed by a welling up of a similar quantity of thin, yellow, odorless pus.

The bladder was thoroughly irrigated and permanently drained. No stone was found at the operation, but a calculus of the size of a pea was discharged one week later.

The patient made an uneventful recovery, constantly secreting large quantities of bile until the spontaneous closure of her fistula a month later.

Cultures and glass-slide smears were taken from the peritoneal exudate outside the bladder, and from both the mucoid fluid and the pus within the bladder.

Bacteriological note.—Both culture and smear from the peritoneum were negative for organisms. The smear from the mucoid fluid showed a very few polymorphonuclear and mononuclear cells, and a considerable number of bacilli, varying from short, thick rod-like forms to longer, thinner

* Read before the Johns Hopkins Medical Society, April 24, 1899.

forms. The smear from the pus showed many pus-cells and a few short, rod-like bacilli. On the agar plates from both the mucoid fluid and the pus was obtained a bacillus in pure culture that corresponded in all its cultural characteristics to the bacillus typhosus. It was actively motile. It decolorized by Gram's method. No gas was formed in glucose-agar. Milk was slightly acidified, reaching its greatest acidity about the second or third day. No indol was formed after one week either in Dunham's solution or in sugar-free bouillon. Flagella, typical of Eberth's bacillus, were demonstrated by Loeffler's method.

Morphology.—The morphology of this organism is so unusual that a full report is taken from the bacteriological notes on three of the media for the first two days:

Twenty-Four Hours: Plain-slant agar; a short to medium long-rod bacillus, occurring singly, in pairs and short chains; rounded ends; staining deeply and evenly, a few staining lightly in centre.

Glucose-Agar: Moderately long bacillus, some plump, some slender; rounded ends; staining very irregularly; some stain deeply full-length, others in the middle only, others on one or both ends, others have nearly lost stain throughout.

Potato: Plump medium-long bacillus; rounded ends; staining very irregularly. Many large swollen forms.

Forty-Eight Hours: Plain-slant agar; medium long-rod bacillus, mostly staining deeply and evenly; many involution forms, some plump and deeply staining, others long, filamentous and very irregularly staining.

Glucose-Agar: An entire loss of normal appearance of the field. The organisms are swollen; only an occasional one takes an even stain, most of them being but shadows or outlines of swollen bacilli. Others stain deeply in centre or on one or both ends.

Many are 4× as long and 2× as thick as normal and show an even faint stain.

Potato: Large plump bacilli with square ends, showing a special tendency to take a half-deep stain through middle and leaving both ends unstained. Many large filamentous forms.

Carter,* two years ago, reported before this society an organism isolated from a patient dead from typhoid fever which showed all the cultural characteristics of the typhoid bacillus but possessed morphological peculiarities similar to those of the organism under discussion. Our bacillus, however, differs from his in showing earlier involution forms, striking changes being observed on agar and potato in 24 hours. On milk, bouillon, and Dunham's solution this organism corresponded morphologically with the control culture of typhoid.

Widal reaction.—Testing with the patient's blood and the organism in question, the reaction was positive with the 1 : 10 and 1 : 40 dilutions, and unsatisfactory with the 1 : 100 dilution. With the known typhoid organism the reaction was positive with the 1 : 100 dilution. With blood from a known typhoid patient in the wards the stock culture of typhoid gave a marked reaction, while the organism in question gave a decided but somewhat less marked reaction in the three dilutions mentioned. Drs. Harris and Schenck very kindly controlled the Widal reactions and were satisfied with the positive character of the results.

Pathogenicity.—A rabbit was inoculated in the ear vein with 1.2 ccs. of a bouillon emulsion made on a 24-hour blood-serum slant culture. The rabbit died in about 30 hours and the bacillus was recovered in pure culture from the œdematous area at the site of inoculation; and, in the order of the greatest number of colonies, from the following organs: gall bladder, peritoneal cavity, right auricle, spleen, kidneys, urinary bladder, right pleural cavity.

Another rabbit, inoculated with 2 minims of a similar emulsion, was ill for several days but fully recovered.

Cushing,* in a paper read before this society one year ago, reported 4 cases, collected from the literature, of post-typhoidal cholecystitis associated with gall-stones which had been operated upon and the bacillus typhosus isolated. To these he added 2 cases from the Johns Hopkins Surgical Clinic.

At the same meeting Dr. Miller† reported a case from the Gynecological Clinic. A short time previously Imhofer‡ had reported a case, and recently Mixter§ has added another.

As a result of clinical and experimental observations on this subject Dr. Cushing proposed the following theory regarding gall-stone formation in these cases of typhoidal cholelithiasis—a theory which had similarly occurred to Dr. Mark W. Richardson.

He summarizes as follows: (1) The bacilli during the course of typhoidal infection quite constantly invade the gall-bladder; (2) the organisms retain their vitality in this habitat for a long period; (3) in the course of time the bacilli are almost invariably found to be clumped in the bile, suggesting the occurrence of an intravesical agglutinative reaction; (4) the clumps presumably represent nuclei for the deposit of biliary salts, as micro-organisms may with regularity be demonstrated in the centres of recently-formed stones; (5) gall-stones being present in association with the latent, long-lived, infective agents, an inflammatory reaction in the viscus of varying intensity may be provoked at any subsequent period.

A brief survey of some of the theories relating to cholecystitis and cholelithiasis in general may be of interest in connection with this report.

Naunyn,‖ in a recent clinical lecture, credits Reidel with holding all cases of cholecystitis dependent upon cholelithiasis; the symtoms, however, of gall-stone colic being due in most, if not in all, cases to the cholecystitis; and, furthermore, this cholecystitis is not an infectious process but follows traumatic irritation by the stone.

* Report of a case of Polybacterial Infection in Typhoid Fever, with Especial Reference to Certain Involutions exhibited by the Bacillus Typhosus.—The Johns Hopkins Hospital Bulletin, No. 75, June, 1897.

* Typhoidal Cholecystitis and Cholelithiasis. Report of a case without previous history of typhoid fever, and Discussion of a possible Agglutinative Reaction in the Bile and its Relation to Stone Formation.—The Johns Hopkins Hospital Bulletin, No. 86, May, 1898.

† The presence of the Bacillus Typhosus in the Gall-bladder Seven Years after Typhoid Fever.—The Johns Hopkins Hospital Bulletin, No. 86, May, 1898.

‡ A Case of Cholecystitis Typhosa. Laparotomie. Heilung.—Prager Medicinische Wochenschrift, 1898. Vol. XXIII, p. 169.

§ A Case of Typhoidal Cholecystitis Associated with Gall-stones; Operation; Recovery.—The Boston Medical Surgical Journal. Vol. CXL., May, 1899, p. 493.

‖ Uber Cholecystitis and Cholangitis Calculosa. Ztschr. f. prakt. Aerzte; Frank, A. M., 1898, VII, 627.

Table I.—*Collected cases of post-typhoidal Cholecystitis associated with Gall-Stones which have been operated upon and the bacillus typhosus isolated.*

	Author.	Sex.	Age.	History.	Operation.	Contents of Gall-Bladder.
I.	Gilbert and Girode, Comptes Rendns de la Soc. de Biologie, 1893, p. 95.	F.	45	Gall-bladder symptoms during fever. Subseqnent gall-stone attacks.	Operator, Ferrier. Cholecystectomy 5 mos. after fever.	Bac. typhosus, pure. Gall-stone. Purulent fluid.
II.	Duprè (Chantimesse's Case), Les infections biliares. Paris Thèse, 1891.	F.	45	No attack with fever. Subsequent gall-stone colic.	Cholecystenterostomy 8 mos. after fever.	Bac. typhosus, pure. Gall-stone.
III.	v. Dnngern, Münch. Med. Woch., June 29, '97.	F.	46	No attack with fever. Subsequent cardialgia. Periostitis of lower jaw in 13 yrs. with bac. typh. Acute gall-bladder attack in 14th year. Widal reaction positive.	Operator, Kraske. Cholecystostomy with evacnation of abscess 14 yrs. after fever.	Bac. typhosus, pure. No stone found, but "probably present." Abscess.
IV.	M. W. Richardson, Bost. Med. and Surg. Jour., Dec. 2, '97.	F.	50	Recent uncertain history of typhoid. Sernm reaction positive.	Operator, M. W. Richardson. Cholecystostomy.	Bac. typhosus, pure. Brownish fluid with bacilli in clumps. Gall-stone in cystic dnct.
V.	H. W. Cnshing, Johns Hopkins Hosp. Bnl., May, 1898.	F.	37	Uncomplicated typhoid 3½ mos. ago. Gall-stone colic with jaundice three weeks ago. Recent peritonitis.	Operator, Prof. Halstcd. Cholecystostomy.	Empyæma of ruptnred gall-bladder which contained numerous small stones. Bacillus typhosus.
VI.	H. W. Cushing, Johns Hopkins Hosp. Bnl., May, 1898.	F.	26	No history of typhoid. Serum reaction positive.	Operator, Prof. Halsted. Cholecystostomy.	Bac. typhosns, pure. Brownish fluid, bacilli in clnmps, gall-stones.
VII.	Richard Imhofer, Prager Med. Wochenschr., 1898, Vol. XXIII, p. 169.	F.	40	Typhoid fever typical, ending 6 weeks previously. Widal reaction.	Operator, Schloffer. Cholecystostomy.	Pus first, then pure bile, a large hazelnnt-sized gall-stone. Pnre cultnre. Bac. typhosus.
VIII.	G. Brown Miller, Johns Hopkins Hosp. Bnl., 1898, Vol. IX, p. 95,	F.	37	Two attacks of gall-stone colic 7 yrs. ago, followed in 1 mo. by probable attack of typhoid fever. Gall-stone attacks ever since.	Operator, Kelly. Cholecystostomy.	Small amount of bile and milky fluid. Two stones. Pnre culture. Bac. typhosus.
IX.	S. J. Mixter, Bost. Med. and Surg. Jonr., May 25, 1899.	F.	60	"Dyspepsia" and occasional vomiting of food for 7 yrs. Positive attack of typhoid ending 6 wks. previonsly.	Operator, Mixter. Cholecystostomy. Choledochostomy.	Turbid bile. 30 gall stones. 2 stones in com. duct. Pure culture. Bac. typhosus.
X.	Writer's Case, Gyn. No. 6682 Feb. 23, 1899.	F.	54	Probable typhoid fever 20 yrs. ago. Widal reaction positive.	Operator, Stokes. Cholecystostomy.	Mucoid clear fluid first, then pns. Stone 1 week later. Bac. typhosus.

Several other post-typhoid cases have been reported without bacteriological notes. These are omitted.

Naunyn calls attention to the fact that all cases of cholecystitis do not have the symptoms of stone. In many other cases diagnosis of gall-stone colic is made *intra vitam*, and abdominal section reveals inflammation of the bladder but no stone in the bladder or passages.

He agrees with Riedel that in many of the so-called gall-stone attacks the symptoms are not caused by wandering of the stones, but by inflammation of the bile passages; but the inflammation is not, as Riedel claims, an aseptic, but a severe infective cholecystitis and cholangitis.

Naunyn calls attention to the chills of cholelithiasis and the spleen and liver tumor that generally accompany the attacks, all of which point to general infection.

Maurice H. Richardson* reports, from a series of 59 operations upon the gall-bladder, 10 cases in which no history of pre-existing gall-stones or of recent acute infectious disease could be obtained. He speaks of these cases of sudden onset in persons of apparently perfect health as "acute accidental cholecystitis." In 4 of his 10 cases no gall-stone was found.

Thus, while we know most cases of acute gall-bladder inflammation to be associated with the presence of stones, we must recognize that some are dependent in no way upon this factor.

The experiments of Netter† and of others demonstrate the liability of the bile to infection after aseptic ligature of the common duct. A catarrhal swelling of the ducts and stasis of the bile might similarly lead to infection and cholecystitis.

The etiology of stone-formation has been a hotly contested question for the past 10 years, the war being chiefly waged in France. On the one side are those, headed by Bouchard,‡

* Acute Inflammations of the Gall-bladder. The American Journal of the Medical Sciences, June, 1898.

† "Présence normale de deux microbes pathogénes, etc." Le Progrès Médical, 1886, p. 992.

‡ Bouchard: "Maladies par ralentissement de la nutrition." Paris, 1882, 6e leçon, p. 79.

who still cling to the old idea of a "special diathesis." Others, with Hanot, believe that the calculi probably have a microbic origin, but diathesis is of preponderating influence. At the other extreme are those who claim a microbic origin for gall-stones and support this view by experimental research. Naunyn* was the first to formulate a theory, holding as probable the infectious origin of biliary lithiasis, and his views have been ably supported in France by such experimenters as Gilbert and his associates, and Mignot.

In this country, Dr. Mark W. Richardson† and Dr. Harvey Cushing‡ have been successful in the experimental production of cholelithiasis.

Mignot,§ after a long series of careful experiments, concludes that the chief factors in the production of biliary lithiasis are: (1) the presence in the gall-bladder of an attenuated organism, of any variety whatever; (2) a relative inertia of the biliary reservoir causing partial stasis and preventing the premature expulsion of soft concretions of cholesterin.

Gilbert,‖ who first reported the experimental production of biliary lithiasis, sounds a warning against the unreserved interpretation of human lithiasis in the same terms. He has recently¶ expressed belief in his ability to cause lithiasis without the intervention of bacteria and by the sole method of a chemical irritation of the vessel walls.

Success in this line, however, would not warrant us in classing human lithiasis as a dyscrasic or toxic process, and we must consider the question sub judice until further investigation throws light upon more of its many problems.

* Naunyn: "Die Gallenkrankheiten." Congrès de Wiesbaden, 1891.

† "On the rôle of Bacteria in the Formation of Gall-stones." Jour. Bos. Soc. Med. Sc., Vol. III, No. 4, Jan., 1899.

‡ Remarks following this paper.

§ "L'origine microbienne des calcules biliaires." Arch. Generales de Mèdicine, 1898, Vol. II, p. 129.

‖ Angiocholitès et cholècystites typhiques expérimentales. Bull. de la Soc. de biologie, Dec. 23, 1893.

¶ Note pour servir à l'historie de la théorie microbienne de la lithiase biliaire. Arch. gen. de Méd., Paris, 1898, II, 257.

OBSERVATIONS UPON THE ORIGIN OF GALL-BLADDER INFECTIONS AND UPON THE EXPERIMENTAL FORMATION OF GALL-STONES.*

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Dr. Hunner's report adds one more to the list of cases in which post-typhoidal gall-stone formation and the persistence of Eberth's bacillus in the gall-bladder have combined to set up a suppurative cholecystitis, demanding operative intervention.

There seems to be little doubt at present but that the original source of infection in these cases is a hæmatogenous one, the bacilli first entering the portal circulation through the atrium afforded by the intestinal lesions. As Fütterer[1] has shown experimentally, organisms so introduced are probably for the most part rapidly eliminated by the liver and thus enter the biliary passages, though many may pass into the general circulation, thus producing a temporary peripheral septicæmia. The frequency of such a typhoidal septicæmia has been demonstrated at this hospital by Dr. Gwyn, who has succeeded in cultivating typhoid bacilli from the blood of eight out of thirty patients examined for this purpose in Dr. Osler's clinic and the occurrence in a variety of situations of peripheral suppurative lesions for which the specific organism of the disease is responsible is thus readily explained.

The belief is quite universal, however, that the biliary infection comes about by ascension and that the organisms enter from the intestine into the common duct. Thus Gilbert,[2] in 1894, held that *B. coli* played the most important rôle in cholecystitis because it was found by him in the duodenum in numbers exceeding all other species and because it was possessed of motile properties which enabled it to enter the common duct. More recently Richardson is quoted by Keen[3] as also expressing a belief in the ascending or intestinal source of infection of the biliary apparatus. He found on one occasion at autopsy "pure cultures of the typhoid bacillus in the gall-bladder, duodenum and jejunum, and it was only when the ileum was reached that colon bacilli began to appear at all." Were the infection an ascending one, I am inclined to believe that other intestinal bacteria from the ileum would have been found associated with the bacillus typhosus in this case.

Recent investigations (unpublished) upon the flora of this part of the intestinal tract have demonstrated, in agreement with the observations of Gilbert and Dominici,[4] that the duodenum, especially of rabbits, is very free from micro-organisms. On one occasion a cubic centimeter of a 24-hour bouillon culture of *B. typhosus* was injected into the ear vein of a rabbit. Two days later from the gall-bladder and duodenum pure cultures of the organism were recovered—a result similar to Richardson's but resultant of course to a hæmatogenous infection. I was not, however, always so fortunate in recovering the organisms. In *Rabbit* IX, which case I will mention later, two days after a similar inoculation into the ear vein, the organisms were not recovered from the bile and in all probability they had been entirely eliminated. I have seen a similar rapid disappearance on direct inoculation into the gall-bladder in dogs. In one animal the bile was sterile twenty-four hours after the inoculation.

Bile itself, contrary to the wide-spread belief in its anti-

* Remarks before the Johns Hopkins Medical Society to accompany Dr. Hunner's report of a Case of Typhoidal Cholecystitis.

septic properties, is a favorable culture medium for most organisms and it is surprising that normal bile should ordinarily be sterile, as Gilbert has demonstrated, when we consider that micro-organisms are in all probability frequently being passed out with it through the liver.

Leubuscher[5] believes that the sterility rests on an unhindered outflow, some degree of obstruction being requisite for the persistence of micro-organisms.

Létienne[6] showed that bacteria are more likely to be present, when there is no disease of the gall-bladder itself, in association with abnormal conditions of the body. In forty-two cases examined he found *Staphylococcus albus* 13 times, *B. coli communis* 13 times, non-liquefying *Staphylococcus* 3 times, *Staph. pyogens citreus, aureus*, etc., 1 each, *B. typhosus, Pneumococcus*, etc., 1 each. On seven occasions the bile was mono-microbic, on 17 poly-microbic, and on 18 sterile. These observations merely show what a highway for micro-organisms the biliary passages are. The observation of Netter[7] is in accordance with Leubuscher's view that ligation of the common duct in animals is followed by an acute inflammation of the biliary passages. Here also the infection is with less likelihood due to an ascending process than to an inflammation induced by micro-organisms, possibly of intestinal origin, which, eliminated by the liver from the portal system, enter the bile ducts from above. Such an infection, however, does not necessarily follow a pathological occlusion of the common duct. Dr. Halsted recently removed a primary carcinoma of the duodenal papilla which had caused complete obstruction. Cultures from the common duct were negative as well as those from the gall-bladder, which was greatly distended by a pale mucoid fluid containing a deposit of fine biliary sand.

The typhoidal lesions, however, offer a portal of entry not alone for the typhoid bacillus but also for all other bacterial inhabitants of the intestine. The *Bacillus coli communis*, for example, which organism, recent observers, as Dreyfuss,[8] Sanarelli,[9] de Klecki[10] and others, have shown to acquire increased virulence in the presence of the inflammatory products of typhoid and other enteritides may similarly enter the portal circulation. This, Dr. Welch[11] demonstrated some years ago to be the case. The colon bacillus, however, apparently rarely passes beyond the liver into the general circulation, its ravages being limited to the confines of the portal system. It consequently may be as frequent a factor and indeed is actually a more frequent agent in the production of post-typhoidal gall-bladder complications than the specific cause of the disease itself. This has recently been emphasized in a paper[12] read before this society.

As was shown in one of the cases reported at that time, there was an active serum reaction toward both *B. typhosus* and the colon bacillus isolated from the gall-bladder. This increased virulence of *B. coli* in many cases of typhoid, being the cause of unusual agglutinative properties of the host's serum toward this organism,* may account for the occasional clumping of *B. coli* in the bile when it has once entered the gall-bladder in correspondence with the reaction toward the bacillus typhosus which seems to be the rule there[19] at some period of the fever.

Salimbini[13] regarded the agglutinating property as one only acquired by the blood-serum after being shed, and expressed a disbelief in its occurrence in the living body. Durham,[14] however, disagrees with this on the ground that numerous observations on peritoneal injections in immunized animals have always shown that agglutination occurs within the peritoneal cavity. Since it has been proven that the bile of typhoid patients acquires agglutinative properties, this reaction *in vivo* in the gall-bladder naturally would occur in a fashion similar to that produced experimentally in the peritoneum. Richardson[19] has examined at autopsy the bile of fatal cases with this in view and found large clumps of bacilli in every case but one (five out of six). It is important to note that the blood-serum of this one case had failed to show an agglutinative reaction during life.

What relation the organisms have toward the deposition of bilirubin calcium and stone-formation has not been conclusively proven. The views of Naunyn[15] are generally accepted, though some of his chemical theories, chiefly that relating to the local production of cholesterin, have been questioned by Chittenden.[16]

The organisms may be present in the gall bladder just as in the urinary bladder during the course of typhoid fever without producing any evidence of cystitis whatever or exhibiting any tendency to become attenuated or to agglutinate, though the patient's serum may give a decided reaction outside of the body.

Just what influence tends to agglutinate the organisms *in vivo* and whether the "clumps" formed really act primarily as the nidus for stone-formation has not been actually demonstrated.

The mere clumping of the organisms in the bile has *in vitro* no macroscopical effect whatever on the bile. I have inoculated bile, aseptically withdrawn from the gall-bladder of animals, with the bacillus typhosus, and subsequently precipitated the bacilli by adding serum from a typhoid patient without producing any appreciable effect on the medium whatsoever.

The mere presence of the micro-organisms in the bile, however, may alone not be sufficient to incite the catarrhal process, the "lithogenous catarrh" of Naunyn, which is generally conceded[17] to be an essential element in the process. I have never been able to produce any such catarrhal process in dogs or rabbits by simple intravenous injection of

* The fact that human serum in health often possesses agglutinative properties toward varieties of *B. coli* probably is only an evidence of an acquired characteristic following an unrecognized invasion of the organism during the course of some preceding enteritis. Such an occurrence has probably been a secret forerunner of most cases of biliary lithiasis; the organisms, being eliminated by the liver, enter the gall-bladder and under certain favoring circumstances produce lithiasis, which after the infectious agent has died out may give no subsequent symptoms. It is not improbable that a chronic enteritis such as may be associated with alcoholism may constantly feed the liver with intestinal bacteria, chiefly *B. coli communis*, and thus ultimately be responsible for the cirrhotic changes which take place there. The demonstration that the organisms found by Adami in cirrhotic livers are colon bacilli would favor this view.

the bacillus typhosus or by injection of the organism directly into the gall-bladder, though the animals have been examined at periods from a few days to several months.

Organisms may be recovered from the gall-bladder long after the original injection, and they frequently are found "clumped," as Blachstein[18] and Welch observed some years ago. The organisms may so remain for an indefinite period without producing any apparent inflammation of the mucosa. To induce this requisite catarrhal process, some other element, presumably some form of irritation such as traumatism or some hindrance to the proper evacuation of the gall-bladder, is necessary.

I am able to show to the society some small biliary calculi of typhoidal origin obtained from the gall-bladders of rabbits, in both cases at the time of inoculation the biliary apparatus having been intentionally maltreated.

On one occasion the organisms (non-attenuated) were inoculated directly into the gall-bladder, which had to be held tightly for some time by a piece of gauze between the fingers to prevent leakage after the syringe was withdrawn. At the autopsy, eight weeks later, three small millet-seed concretions were found adherent to the mucosa of an inflamed thickened and distended gall-bladder.

The second case (RABBIT IX of our series) is as follows:

March 17, 1898. Inoculation of 1 cc. of 24-hour bouillon culture of *Bac. typhosus* into ear vein.

March 19. Laparotomy. No evidence of inflammation. Cultures and cover-slips from gall-bladder and duodenum were negative for micro-organisms. Considerable traumatism of gall-bladder.

March 21. Second inoculation of 1 cc. of 18-hour culture of *Bac. typhosus* into ear vein. Animal quite ill subsequently, but recovered.

June 13. Widal reaction positive. Laparotomy. Marked evidence of cholecystitis. Gall-bladder bound up by adhesions in lappets of liver and identified with difficulty. One cc. of pale bile aspirated from gall-bladder. Stained preparations showed a few rod-shaped organisms. Culture=*Bac. typhosus.*

June 14. Animal found dead. Autopsy. Peritonitis. Serosa greatly bile-stained. Gall-bladder thickened, congested and densely adherent to liver. Contents: Small amount of pale mucoid material, and three gall-stones. The largest is dark-colored, somewhat irregular in shape, measuring 3 mm. in its longest diameter.

Decomposition had set in and bacterial observations were not made.

Possibly such a concretion may be regarded merely as a precipitation and not a true crystallization though it possesses the characteristics of a young biliary calculus having a marked cholesterin covering. The stone depicted by Richardson[19] and the early calculi described by Gilbert and Fournier[20] were evidently of this character. The concretions were regarded as stones in the primary stages of development. Their chief constituents are bile pigments combined with calcium. These bilirubin calcium concretions are less commonly found in the human gall-bladder where stones ordinarily contain a large predominance of cholesterin. Chittenden[16] says that bovine gall-stones possess this same characteristic and are often pure-pigment calculi, sometimes wholly without cholesterin.

Although Galippe,[21] as early as 1886, advanced the theory of a microbic origin of lithiasis in general, the chief credit of the demonstration of the infectious nature of cholelithiasis belongs to Gilbert. The results of his observations, begun in 1890,[22] were utilized by Naunyn[15] at the Wiesbaden Congress in 1891, when he advanced his hypothesis on biliary infections. Since that time Gilbert, and his collaborators, Girode, Dominici, Claude and Fournier, have continued to publish the progress of their interesting and valuable investigations on the relation of infectious processes to diseases of biliary apparatus.

Experimental attempts to produce calculi of infectious origin were for a long time unavailing. In 1893[23] they first noted the presence of "*petites concrétions verdâtres*" which had formed during a typhoidal cholecystitis in a rabbit. Following this discovery, methodical attempts were made for a number of years to obtain more perfect and undoubted concretions. On January 29, 1897, these efforts were rewarded by the formation of a definite stone obtained from the gall-bladder of a dog previously inoculated with the *Bacillus coli communis.*[22]

Gilbert and Fournier, however, failed to announce their results until after Mignot, who had entered the same field of work, had presented to the Societé de Chirurgie, on the 19th of May, 1897, three small experimental calculi formed in a guinea-pig by *Bacillus coli.*[24] It was generally believed that the bacillus of Escherich played the most important part in these infections. Interest in typhoidal cholecystitis, however, led Gilbert to experiment with Eberth's bacillus and on October 30, 1897, he with Fournier,[20] profiting by Mignot's idea of attenuation, reported the production of biliary calculi in a rabbit resultant to an infection with *B. Typhosus.*

These calculi were regarded as stones in the primary stage of their development and from the description they must have resembled closely those produced by Richardson[19] and those shown to this society. The gall-stones, however, which Mignot succeeded in producing experimentally were said by Hartmann[24] and acknowledged by Gilbert[27] to have been identical in appearance with those commonly seen in human gall-bladders. These calculi were presumably five or six months old.

Various experimenters have adopted different methods in their attempts to produce infectious cholelithiasis. Endeavors to modify the composition of the bile and to alter the mucosa of the gall-bladder and to produce in divers ways a biliary stasis have equally been unrewarded.

The mere introduction of virulent micro-organisms alone as well as the introduction of aseptic foreign bodies[25] without micro-organisms have similarly been unsuccessful. Mignot claimed that one of the two conditions essential to the formation of calculi was the extreme attenuation in virulence of the microbe employed, and regarded the degree of virulence of the organism as more important than the species. Adopting this principle, Gilbert and Fournier,[20] by inoculating cultures of colon or typhoid, previously attenuated by heat, directly into the gall-bladder, were rewarded by finding some months later definite calculi, from the centres of which they recovered the original organisms.

This preliminary attenuation of the infective agent which

Mignot has found esssential to the process may possibly, under certain conditions, take place in the body and be analogous to the agglutination of the organisms which takes place in the gall-bladder; the clumps, according to Richardson's hypothesis, forming the primary nidus of deposition for the biliary salts and pigments. In his attempt to form stones on this principle he inoculated an agglutinated culture of *Bacillus typhosus* directly into the gall-bladder of a rabbit and was successful on one occasion in producing a fair calculus.

Mignot,[26] however, claims that to produce true stratified calculi five or six months are requisite, and that a second condition, as important as the attenuation of the micro-organisms, is necessary, namely, the prevention of the premature expulsion of the soft concretions. This he accomplished in various ways. In his most recent article two especially characteristic cases are described.

In one of them the gall-bladder was tamponed in the presence of colon bacilli for one month. At the end of that time the tampon was removed and the gall-bladder closed. Fourteen months later, 7–8 faceted stones were found occupying the gall-bladder which presented the anatomical picture characteristic of old gall-stone cases.

In another case two gall-stones were made to form about a thread which was fastened into the wall of a gall-bladder previously inoculated with attenuated colon bacilli. Dr. John Homans[28] has reported a clinical experience similar to this experimental one in which at a second operation for cholelithiasis, gall-stones were found to have formed about the threads used at the primary operation in suturing the gall-bladder to the abdominal wall. There is no accompanying bacteriological note, unfortunately. These were large cholesterin stones such as Mignot has succeeded in producing and were found twenty months after the primary operation.

Mignot believes that the process of stone-formation and increment in the size of stones ceases with the death of the micro-organisms. Stones found in the gall-bladder are presumably on most occasions all of the same age, and always possess the same appearance, chemical composition and bacteriological characteristics. The original condition favorable to their formation, therefore, seems to be a transitory one. Old calculi are usually sterile, though their nuclei may contain the faintly-staining shadow of bacilli. Recently-formed stones contain micro-organisms. Mignot further believes that if stones in process of development are removed the chances are in favor of a new formation. This is an argument against the so-called "ideal" operation and justifies the clinical experience of most surgeons that it is preferable to drain the gall-bladder in recent cases till one is practically sure of the aseptic condition of the bile and convinced that the ducts are sufficiently patent to allow of the free escape of the contents of the gall-bladder. It is surprising that one does not more often encounter secondary formations of gall-stones after preliminary operations, when we consider that the combination of traumatism and necessarily-retained micro-organism is present, a combination most favorable for the experimental production of stones.

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NOTE ON NEW BOOKS.

A Clinical Text-Book of Medical Diagnosis for Physicians and Students. Based on the most recent methods of examinations. By OSWALD VIERORDT, M. D. Authorized translation, with additions by FRANCIS H. STUART, A. M., M. D. Fourth American edition from the fifth German; revised and enlarged, with one hundred and ninety-four illustrations. (*Philadelphia: W. B. Saunders*, 1898).

The appearance of a fourth American edition from the fifth German of Vierordt's "Medical Diagnosis," might seem to call only for general remarks on the merits and evident popularity of the work. It has been in its way so long a standard text-book that it hardly requires an introduction to American readers.

The principal additions mentioned by the author in his preface to this edition, have been made in the sections treating of gastric digestion and diseases of the nervous system. A few things might still have been added; for example, there is here no mention of Turck's gyromele, or of several other apparatuses that have fully as much value as diagnostic appliances as some of those noticed at length. In the section on the nervous system the occasionally very confusing nervous symptoms of chlorosis appear to be unnoticed, which is an important omission. Other deficiencies might be pointed out, but in most respects the work seems well up to date, and a useful addition to any physician's library. The illustrations are well selected and generally very helpful; in this regard the work has a decided advantage over some other text-books on medical diagnosis.

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Studies on Reactions to Stimuli in Unicellular Organisms. II.—The Mechanism of the Motor Reactions of Paramecium. IV.—Laws of Chemotaxis in Paramœcium. By Herbert Jennings. Reprinted from the American Journal of Physiology, May, 1899.

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Thomas McCrae, M. B., Instructor in Medicine.
Albert C. Crawford, M. D., Assistant in Pharmacology.
Sidney M. Cone, M. D., Assistant in Surgical Pathology.
Norman MacL. Harris, M. B., Assistant in Bacteriology.
Jesse W. Lazear, M. D., Assistant in Clinical Microscopy.
Stewart Paton, M. D., Assistant in Clinical Neurology.
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Elizabeth Hurdon, M. D., Assistant in Gynecology.
Henry O. Reik, M. D., Assistant in Ophthalmology and Otology.
William G. MacCallum, M. D., Assistant in Pathology and Curator of the Museum of Pathology.
Percy M. Dawson, M. D., Assistant in Physiology.
Louis P. Hamburger, M. D., Assistant in Medicine.
Melvin T. Sudler, Ph. D., Assistant in Anatomy.
Norman B. Gwyn, M. B., Demonstrator in Clinical Microscopy.

GENERAL STATEMENT.

The Medical Department of the Johns Hopkins University was opened for the instruction of students October, 1893. This School of Medicine is an integral and coördinate part of the Johns Hopkins University, and it also derives great advantages from its close affiliation with the Johns Hopkins Hospital. The required period of study for the degree of Doctor of Medicine is four years. The academic year begins on the first of October and ends the middle of June, with short recesses at Christmas and Easter. Men and women are admitted upon the same terms.

In the methods of instruction especial emphasis is laid upon practical work in the Laboratories and in the Dispensary and Wards of the Hospital. While the aim of the School is primarily to train practitioners of medicine and surgery, it is recognized that the medical art should rest upon a suitable preliminary education and upon thorough training in the medical sciences. The first two years of the course are devoted mainly to practical work, combined with demonstrations, recitations and, when deemed necessary, lectures, in the Laboratories of Anatomy, Physiology, Physiological Chemistry, Pharmacology and Toxicology, Pathology and Bacteriology. During the last two years the student is given abundant opportunity for the personal study of cases of disease, his time being spent largely in the Hospital Wards and Dispensary and in the Clinical Laboratories. Especially advantageous for thorough clinical training are the arrangements by which the students, divided into groups, engage in practical work in the Dispensary, and throughout the fourth year serve as clinical clerks and surgical dressers in the wards of the Hospital.

REQUIREMENTS FOR ADMISSION.

As candidates for the degree of Doctor of Medicine the school receives:

1. Those who have satisfactorily completed the Chemical-Biological course which leads to the A. B. degree in this university.

2. Graduates of approved colleges or scientific schools who can furnish evidence: (*a*) That they have acquaintance with Latin and a good reading knowledge of French and German; (*b*) That they have such knowledge of physics, chemistry, and biology as is imparted by the regular minor courses given in these subjects in this university.

The phrase "a minor course," as here employed, means a course that requires a year for its completion. In physics, four class-room exercises and three hours a week in the laboratory are required; in chemistry and biology, four class-room exercises and five hours a week in the laboratory in each subject.

3. Those who give evidence by examination that they possess the general education implied by a degree in arts or in science from an approved college or scientific school, and the knowledge of French, German, Latin, physics, chemistry, and biology above indicated.

Applicants for admission will receive blanks to be filled out relating to their previous courses of study.

They are required to furnish certificates from officers of the colleges or scientific schools where they have studied, as to the courses pursued in physics, chemistry and biology. If such certificates are satisfactory, no examination in these subjects will be required from those who possess a degree in arts or science from an approved college or scientific school.

Candidates who have not received a degree in arts or in science from an approved college or scientific school, will be required (1) to pass, at the beginning of the session in October, the matriculation examination for admission to the collegiate department of the Johns Hopkins University, (2) then to pass examinations equivalent to those taken by students completing the Chemical-Biological course which leads to the A. B. degree in this University, and (3) to furnish satisfactory certificates that they have had the requisite laboratory training as specified above. It is expected that only in very rare instances will applicants who do not possess a degree in arts or science be able to meet these requirements for admission.

Hearers and special workers, not candidates for a degree, will be received at the discretion of the Faculty.

ADMISSION TO ADVANCED STANDING.

Applicants for admission to advanced standing must furnish evidence (1) that the foregoing terms of admission as regards preliminary training have been fulfilled, (2) that courses equivalent in kind and amount to those given here, preceding that year of the course for admission to which application is made, have been satisfactorily completed, and (3) must pass examinations at the beginning of the session in October in all the subjects that have been already pursued by the class to which admission is sought. Certificates of standing elsewhere cannot be accepted in place of these examinations.

SPECIAL COURSES FOR GRADUATES IN MEDICINE.

Since the opening of the Johns Hopkins Hospital in 1889, courses of instruction have been offered to graduates in medicine. The attendance upon these courses has steadily increased with each succeeding year and indicates gratifying appreciation of the special advantages here afforded. With the completed organization of the Medical School, it was found necessary to give the courses intended especially for physicians at a later period of the academic year than that hitherto selected. It is, however, believed that the period now chosen for this purpose is more convenient for the majority of those desiring to take the courses than the former one. The special courses of instruction for graduates in medicine are now given annually during the months of May and June. During April there is a preliminary course in Normal Histology. These courses are in Pathology, Bacteriology, Clinical Microscopy, General Medicine, Surgery, Gynecology, Dermatology, Diseases of Children, Diseases of the Nervous System, Genito-Urinary Diseases, Laryngology and Rhinology, and Ophthalmology and Otology. The instruction is intended to meet the requirements of practitioners of medicine, and is almost wholly of a practical character. It includes laboratory courses, demonstrations, bedside teaching, and clinical instruction in the wards, dispensary, amphitheatre, and operating rooms of the Hospital. These courses are open to those who have taken a medical degree and who give evidence satisfactory to the several instructors that they are prepared to profit by the opportunities here offered. The number of students who can be accommodated in some of the practical courses is necessarily limited. For these the places are assigned according to the date of application.

During October a select number of physicians will be admitted to a special class for the study of the important tropical diseases met with in this region.

The Annual Announcement and Catalogue will be sent upon application. Inquiries should be addressed to the

REGISTRAR OF THE JOHNS HOPKINS MEDICAL SCHOOL, BALTIMORE.

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THE GROWTH AND REGENERATION OF THE TAIL OF THE FROG LARVA*

STUDIED WITH THE AID OF BORN'S METHOD OF GRAFTING.

By Ross Granville Harrison, *Associate Professor of Anatomy, Johns Hopkins University, Baltimore.*

In the method of grafting we have a means of experimentation for which no substitute is offered. Born's discovery that certain amphibian embryos lend themselves with readiness to such operations, is of especial importance in that it renders the method applicable to the study of developmental problems. How important this form of experiment is, may be well appreciated from a careful study of the paper in which Born records the results of his work in this field.

In the spring of 1897 I instituted a number of experiments according to Born's method upon the embryos of several of to our American frogs, which were found to be well adapted the purpose. An account of these experiments is here given.

The embryos of two of the forms used differ so markedly in coloration, that in any case where parts derived from each are united together into a single organism one may follow in the living specimen, as development proceeds, the movement of any group or layer of cells with respect to the original dividing line between the two constituents. By varying the region in which the parts are stuck together it thus becomes possible to trace out the mode of growth of individual structures or organs.

These circumstances were taken advantage of in a series of experiments which are described here in the second section. They concern more especially the normal mode of growth of the tail from the time when the medullary folds are closed over and the tail bud is just formed; they form therefore the basis for the study of the later phases of development, beginning with the stage at which nearly all previous accounts leave off. During the development of the tail a remarkable shifting of the epidermis over the underlying organs was observed to take place. This was followed in some detail since it is of importance in explaining the mode of distribution of cutaneous nerves in the adult.

Another series of experiments, referring to the regeneration of the tail, was made with the special object in view of ascertaining to what extent the oral end or pole of the amputated tail rudiment is capable of regenerating. These are described in the third and fourth sections.

Finally, in the fifth section some scattered observations upon the fate of the tissues in the heteroplastic combinations are recorded.

The matter is thus considered under the following headings:

I. Material and Methods.

II. The Growth of the Tail and its Bearing upon the Mode of Distribution of Cutaneous Nerves.

III. The Regeneration of the Tail.

IV. The Regeneration of the Reversed Tail.

V. Reactions between Tissues Derived from Different Species.

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*Reprinted from the "Archiv für Entwickelungsmechanik der Organismen," VII. Band.

I. Material and Methods.

In the vicinity of Baltimore the spawn of various amphibia may be obtained in great abundance. For the purpose of experiment I made use of the embryos of Amblystoma punctatum, and of several species of frog, including Rana sylvatica, R. virescens (halecina), and R. palustris. The embryos of Amblystoma, however, are not at all adapted for transplantation experiments for the reason that their wound-healing power is but very slight. Since the yolk oozes out when laid bare instead of being quickly covered again by the overgrowth of the ectoderm, the whole embryo eventually macerates in consequence even of simple operations.*

Of the three anouran species used all possess the power of rapid wound-healing which is the chief essential to successful grafting. For the present purpose the most fortunate combination between two species is that of R. palustris and R. virescens, on account of the very sharp color contrast, and the absence of undue difference in size between them. The eggs and embryos of the former are of a light yellowish-brown color, while those of the latter are dark brown, almost black. The coloration is due partly to the embryonic pigment situated for the most part in the ectoderm cells, and partly to the yolk granules, which are scattered throughout all the tissues. In R. palustris the latter are of a decided yellowish hue, while in R. virescens they are light-drab or almost white. The contrast between the two species is sharpest in the cells of the epidermis. In any combination of embryos of the two forms it is possible to distinguish in this layer the species from which every single cell is derived. In the structures underlying the epidermis the sharpness of the contrast is somewhat obscured (especially for the first day or two after union) by the imperfect transparency of the tissues. But even in the endoderm or in the axial musculature the specific coloration of the cells may be clearly made out. The distinguishing characters persist for ten days or more after grafting, and during this period many important developmental changes take place. After the expiration of this time the absorption of the yolk granules and the disappearance of the embryonic pigment from the epidermis cells make it more difficult to distinguish between cells of the two species. The perceptible differences between the two then no longer extend to each individual cell. This is true with regard to color differences, upon the existence of which the method is largely dependent, for the specific markings of older larvae are due to the characteristic groupings of the large mesenchymal chromatophores, rather than to differences in their individual form and color.

The embryos which were made use of in all the grafting experiments were in that stage of development in which the medullary folds are entirely closed over, and the tail bud is well rounded off from the trunk (Fig. 2).† In this stage the embryos of R. virescens are about 4 mm. in length, while those of R. palustris are slightly longer.

The spawning period of R. virescens is short. In the spring of 1897 it lasted but about ten days (March 22 to April 1). The first eggs of R. palustris were found on April 1. For this reason it was necessary to resort to ice for the purpose of arresting development and prolonging the season during which grafting experiments could be carried on. The eggs were kept at a temperature just a little above freezing point of water without undergoing deterioration. They made but little perceptible advance in development during the five weeks they were retained.

Concerning the methods employed in transplantation, there is but little to add here to Born's account. In but one essential did the method pursued in the present research differ from his. That is, cool tap water was used instead of salt solution, as the medium in which the operations were performed. The former has two distinct advantages over the latter. In the first place it obviates the necessity of bringing the larvae back to their normal medium after operation and healing in salt solution. This, according to Born's experience, must be done very gradually and is a rather tedious process. The second and more weighty objection to the use of salt, is that the larvae show the effect of their treatment both in retardation of development and in general weakness.* It is true that a larger proportion of experiments are successful initially when the operation is performed in salt solution, in which the wounds heal more quickly and surely. But the much larger percentage of healthy and vigorous tadpoles which survive in the end, when only cool, fresh water is used, more than compensates for the cases unsuccessful at the start. Nevertheless in any case, one must expect to lose many promising composite individuals, and very often, as Born points out, from causes apparently unassignable.

The method of study consisted largely in the daily observation upon the living specimen, although a quantity of material was preserved for histological investigation. The figures in the text (except Figs. 1, 14 and 18) are all reproduced from outline drawings of the living tadpoles made with the camera lucida. One experiences considerable difficulty in sketching the larvae by means of the camera, for it is almost impossible to keep them perfectly still. Care was taken, however, that the important parts (in most cases the tail) should be made perfectly accurate. In some cases the body and head were afterwards drawn in from preserved specimens.

The photographs reproduced in Plate X were made from the living tadpoles. Those of the four frogs (Pl. XI) were taken from specimens preserved in formaldehyde. For the purpose of photographing live tadpoles the apparatus, originally intended for photomicrography, was arranged as shown in the diagram (Fig. 1).† The larvae were put into a glass cell (*a*) having vertical plane walls and filled with water. This was placed directly between the camera (*c*) and the source of the light (*l*), an arc light of four thousand candle power.

* Born had the same difficulty with Triton embryos.

† This is perhaps a slightly older stage than that which Born found to be most advantageous.

* Born mentions that operations of less difficult nature may be successfully performed in water. He also calls attention to the ill effects of keeping the larvae too long in salt solution. For a special study of the influence of salt solution upon the development of amphibia, which was first noted by Morgan (18), see Hertwig (10) and Wilson (28).

† This apparatus has been described in full by Hoen (11).

This could be so adjusted by screwing from side to side that the rays, made parallel by passing through the condenser (*d*), were directed so as to pass somewhat obliquely to one side of the water-chamber, to the surface of a plane mirror (*m*), which was placed so as to reflect the light to the surface of the tadpole turned towards the camera. At the same time a small amount of diffuse light passed through the glass cell and likewise through the tail of the larva. The strong reflected light was to bring out the surface markings, while the transmitted light gave a transparent effect to the tail. Naturally, a great deal of experimentation was necessary before the proper proportions of reflected and transmitted light could be determined. The difficulty was increased by

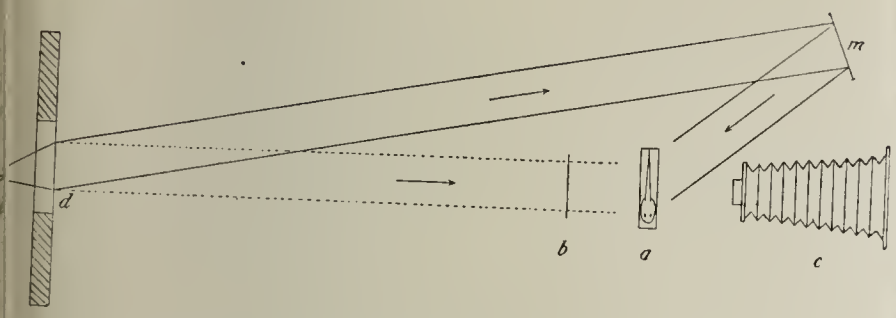


Fig. 1.—Diagram showing method of illumination used in photographing living tadpoles. Explanation in text.

the fact that this proportion is different for each tadpole, since it depends upon the deepness of pigmentation. The intensity of the reflected light was found to be best left at its maximum, while that of the transmitted could be most conveniently regulated by the interposition of colored screens (*b*) of different actinic power. Exposure of several seconds upon very sensitive plates was necessary to bring out surface markings properly. This accounts for the blurred appearance of the mouth parts in the majority of the figures.*

II. The Growth of the Tail and its Bearing upon the Mode of Distribution of Cutaneous Nerves.

It is the generally accepted view that the tail of the vertebrate embryo increases in length by a process of apical growth. There is no doubt that the new muscle plates are added at the tip, and it is here that the notochord and spinal cord remain undifferentiated and contain numerous cells in process of division as evidence of active growth.

In the method of combining parts of differently pigmented embryos we have a means of testing whether the accepted view is correct as regards each of the individual constituents of the tail. For this purpose the following experiment may be made: The tail of an embryo of R. palustris is cut off and transplanted to the body of a virescens embryo in place of its own tail, which has previously been removed. The cut is best made in an oblique direction with respect to the axis of the body in a line passing just distal to the anus (Fig. 2).* The wound heals very readily after this light operation, but owing to the sharp contrast in color between the tissues of the two species the transplanted tail may be distinguished from the body even by the naked eye.

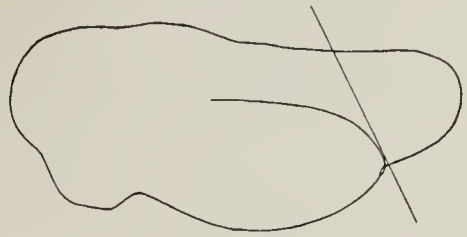


Fig. 2.—Rana virescens in grafting stage, showing cut made when tail alone is to be replaced. × 11.

I give below the history of an individual case, the one from which the figures were made.

On the day after the operation the epidermis of the trunk (R. virescens) extends out over the base of the tail (R. palustris). The light ectoderm (stippled area, Fig. 3) of the grafted tail has increased in extent as compared with the day before, but not commensurately with the increase in length of tail, which is now considerably longer than at the time of operation. Two days after a still larger portion of the base

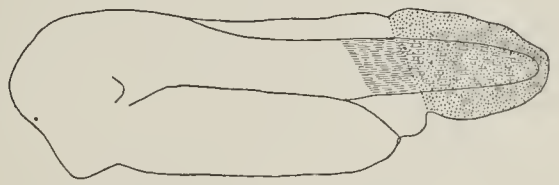


Fig. 3.—Same larva as in Fig. 2, thirty hours after operation. Virescens tissue simply outlined; palustris epidermis stippled; palustris musculature shaded. × 11.

of the tail is covered by the same epidermis as the body, so that at this time but little over half of the tail is covered over by the transplanted epidermis (Fig. 4). On the fourth day, the length of the tail having continued to increase, the area

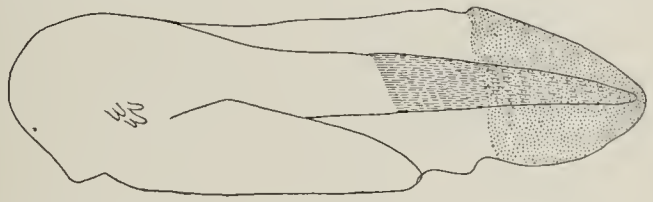


Fig. 4.—Same larva, fifty-three hours after operation. × 11.

of light-brown ectoderm becomes still further removed from the base. The line of demarcation still retains its oblique direction in a general way, but is becoming wavy or jagged, and is as a whole somewhat curved where it passes over the axis of the tail, the convexity being turned towards the distal end (Fig. 5). This is noticeable in all cases, though in a varying degree. On each following day the ectoderm of the

* It gives me great pleasure to express here my obligation to Mr. A. S. Murray for much invaluable aid given in connection with the work of photography.

* The oblique cut is preferable to the transverse in that it affords an easy means of distinguishing the dorsal edge of the small piece from the ventral.

trunk moves further and further out over the tail, the boundary between the two kinds of epidermis becoming more irregular and jagged (Fig. 6). The epidermal cells of the body do not cover up or replace those of the tail, however, for the surface covered by the latter continues to increase in absolute amount. By the eighth day or, in some cases, earlier, nearly two-thirds of the tail are covered by cells which have shifted to it from the body (Fig. 7). After the expiration of this time there is only a slight further change in the position of the line of demarcation. It may be made out in some cases for a week longer. Then, owing to the disappearance of yolk granules and of pigment from the epidermis cells, it becomes practically impossible to distinguish between the cells of the two species.

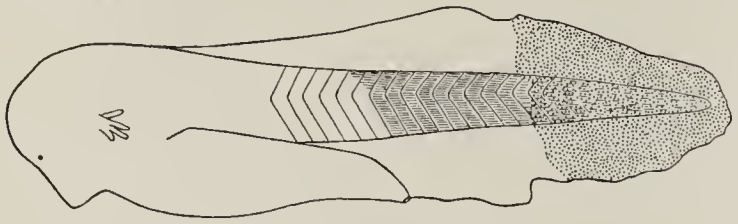


Fig. 5.—Same larva, seventy-seven hours after operation. ×11.

In all, twenty cases were observed and without exception the changes just described took place, and in exactly the same manner in the reciprocal experiment where a virescens tail was grafted to the body of a palustris embryo. In a number of cases the tails of two larvae were merely interchanged, so that an exact comparison could be instituted.

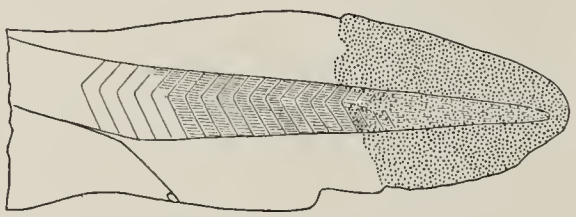


Fig. 6.—Tail half of same larva, five days after operation. ×11.

The changes in position of the boundary between the integument of the two components is due beyond a doubt to actual shifting of the cells and not to any mere diffusion of pigment granules. This may be clearly demonstrated by examining the border under moderate magnifying power with strong reflected light. This brings into view the individual cells. Those of each component maintain absolutely their specific coloring without there being any intermingling of pigment granules whatever. The boundary line is a zigzag one, the two kinds of cells being neatly fitted to one another.*

With regard to the structures underlying the epidermis the changes of relative position which take place during growth are not so marked as in the epidermis itself. On the day after the operation the larva is still very opaque, but even then, with proper illumination, something of the deep-lying tissues, more especially the muscle plates, may be made out. The line of demarcation between the muscle tissue of the virescens constituent (outlined in the figures) and that of the palustris tail (shaded in the figures) is seen to have remained at the base of the tail, very near to where it was just after the operation, while the epidermis of the body has crept some distance out beyond its original territory (Fig. 3). Three days after the

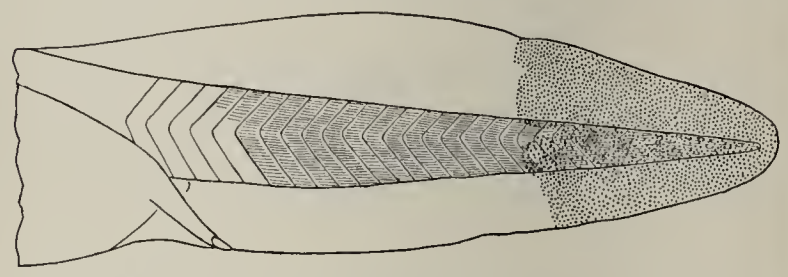


Fig. 7.—Tail half of same larva, seven days after operation. ×14.

operation the individual muscle plates may be observed. The oblique cut made in operating has evidently affected several segments, for at least two of them are made up partly from each component. These two are nevertheless perfect in form (Fig. 5). During the three days the position of the junction between the two parts has moved slightly away from the head as compared with the position of the anus, regarded as a fixed point. This relative movement continues slowly (Fig. 6) until, about the eighth day, it amounts approximately to the length of three segments. The point of union, as seen on the ventral edge of the muscle plates is now considerably distal to the anus (Fig. 7), while a perpendicular drawn through the anus at this stage strikes the posterior part of the eleventh segment (counting from the head) instead of the fourteenth as at the time of operating. This change of position is due to the relative increase in the length of the individual muscle plates as compared with the length of the body (from nose to anus), which latter, as may be seen from the comparison of the sketches (Figs. 2–5), expands but slowly. Measurements made from sections of larvae preserved in stages corresponding to those shown in Fig. 2 and Fig. 7 demonstrate that the average length of the myotomes increases during this time about seventy per cent. of the original length, while the distance from the pituitary body to the anus (projected upon the notochord) increases but about forty per cent. This shows that differences in amount of interstitial growth will account for the relative change of position. Besides, as is well known, intercalation of myotomes during development and additions to the series from the cranial end have not been observed to take place. The shifting of the muscle plates out from the trunk to the base of the tail is accentuated in appearance by the increase in breadth of the fin-fold, by which the anal opening is removed to a considerable distance ventral to the limit of the muscle plates.

The growth of the notochord apparently keeps pace with that of the series of myotomes, and is due, as is well known, largely to apical growth. Further evidence of this is to be had from these experiments, for in grafting it is very seldom that the tissues of the notochord of the two components actually fuse together. They remain separated by connective tissue; the blunt ends where they abut against one another bend slightly

* The shifting of the epidermis may likewise be demonstrated by following the movement of a scar during development. Byrnes (4) found that scars made in the region of the hind legs in embryos in the stage shown in Fig. 2 gradually pass out towards the tip of the tail.

to one side.* During the growth of these transplanted tails it is in the distal piece of chorda that by far the greatest amount of increase in length takes place. The point of union of the two parts of the chorda dorsalis remains by the junction between the myotomes of the two components. The relative amount of interstitial and apical growth is, therefore, the same in both notochord and axial musculature.

Regarding the growth of the spinal cord the present experiments do not adduce new evidence. Its tip keeps up with the tip of the notochord as the tail grows. There is such complete union of the two portions of spinal cord in the healing of the wound after grafting that no scar remains as a landmark. That the greater amount of growth takes place from the end is, however, certain from the well-known fact that the interstitial growth does not keep pace with that of the vertebral column and segmental musculature, the circumstance which leads to the formation of the cauda equina.

The shifting of the epidermis tailwards over the underlying organs is not confined merely to the tail, as further investigation shows. In another series of experiments, instead of grafting only the tail to the body of another larva, a small portion of the trunk, say about four segments, including a portion of the yolk mass, was transplanted to the body of a larva of the other species, from which the same amount had been cut off. In such cases on the day after the operation the epidermis of the body has moved slightly towards the tail over the underlying tissues of the other component (Fig. 8).†

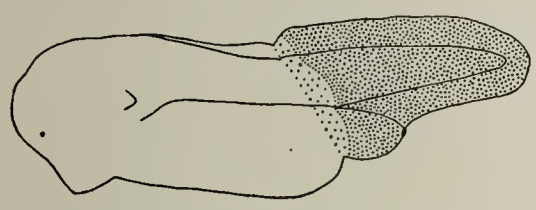


Fig. 8.—Rana virescens with tail and small portion of trunk replaced by palustris tissue, twenty-six hours after operation. Palustris epidermis densely stippled; palustris yolk and mesoderm covered by viresceus epidermis lightly stippled. × 11.

Four days after the operation the amount of shifting is so considerable that even the base of the tail is covered with the dark skin. The line of demarcation (between lightly and heavily stippled areas in the figures), originally straight, now takes a very characteristic sharp bend at the level of the middle of the muscle plates, so that while the dorsal portion passes ventrally and tailwards, the ventral portion has a ventral and cranial direction (Fig. 9). The skin of the dorsal half has moved further than that of the ventral. It seems probable that the movement is held in check ventrally by the opening of the alimentary tract, where the epidermal cells are continuous with the cells lining the cloaca. In the underlying organs some changes have also occurred. The muscle plates of the posterior component are pushed further towards the tail as compared with the yolk. The limit between the muscle tissue of the two parts retains its original direction, but between the two kinds of yolk this is not the case, for here the boundary is either nearly perpendicular or runs ventrally and headwards. The shifting of the epidermis continues until the integument of the anterior component extends to a point just beyond the anus ventrally, while dorsally a considerable stretch of the tail is covered by it. In amount, the movement is considerably less in this region than further towards the tip of the tail, as demonstrated in the first series of experiments.

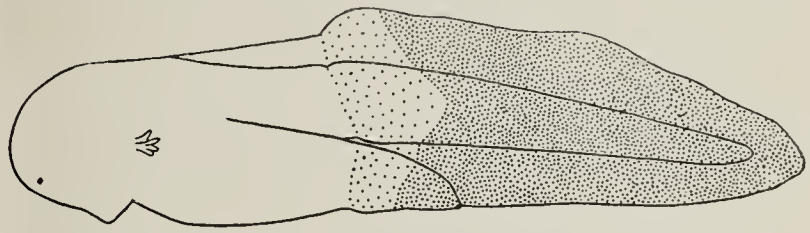


Fig. 9.—Same as Fig. 8, four days after operation. × 11.

Even in the region of the pronephros and forelimb there is a slight change in position of the ectoderm with respect to the underlying organs as development proceeds. This is clearly shown in specimens in which the two constituents are united in this region. After the expiration of a week the position of the border between the two kinds of skin may be observed to have shifted somewhat in the same direction as in the posterior part of the trunk and tail, though relatively much less in amount.

The explanation of this general movement of the epidermis from the head towards the tail is to be sought in the absence from this tissue of any definite growing point such as is found at the tip of the axial organs of the tail. At least, if there is a greater proliferation of cells in the epidermis of the tip than elsewhere over the body, it is not sufficient to keep pace with the general increase in length. A glance at the figures used in the foregoing description shows that during the one week in which this shifting takes place, the tail grows from almost nothing to a length greater than that of the rest of the animal (cf. Figs. 2, 5 and 7). The consequence of this rapid growth is a steady pulling of the covering of the body out to the tail, since the attachment of the epidermis to the underlying tissues must offer but insufficient resistance to this movement. The greatest amount of shifting is found in the cells nearest to the tip, and it becomes less and less as the head is approached. A given cell located originally at the posterior limit of the fourteenth myotome moves during seven days to a point at least 2.5 mm. further peripherally, that is, through a distance equal to about fourteen segments. Of course it is probable that a certain amount of the movement is due to the protoplasmic activities of the ectoderm cells themselves, as we have good evidence of the amoeboid activity of such cells, especially in the covering of wounds, and in fact when the tail is amputated.*

* Cf. page 186. Also Born, l. c. page 394.

† For a day or two after the operation in such cases a very marked constriction where the two portions of yolk join may be observed. This disappears entirely in the course of time, and the composite larva assumes a normal appearance.

* The covering of the wounds through the amoeboid activity of epidermis cells was first demonstrated by Peters (20) in the case of the frog's cornea. Barfurth (2) confirmed this result in his study of wound-healing after amputation of the tail.

To sum up, then: The tail of the tadpole increases in length by a process of apical growth in the musculature, notochord and spinal cord, and also, but to a much less extent, by the greater amount of interstitial growth of these parts as compared with that of the body as a whole; this latter factor results in the pushing of about three segments from the body to the base of the tail. Little or no evidence of apical growth is to be found in the epidermis, which gradually moves out from the body to the tail, so that finally two-thirds of the latter become covered by skin from the body.*

The gliding of the skin over the underlying organs is a most interesting phenomenon when considered in connection with the mode of distribution of the cutaneous nerves in the adult vertebrate.

As is well known, the integument of the trunk is divisible into a series of zones, each of which corresponds to the area of distribution of a given spinal nerve. There is an overlapping of adjacent zones, but the sensory areas of the individual nerves are continuous, at least in those portions of the trunk left undisturbed by the growth of the extremities. The portion of the skin innervated by a given spinal nerve does not necessarily exactly overlie the muscular zone which is supplied by the ventral root of the same nerve. In the region of the first dorsal vertebra the limits of the sensory and motor belts do correspond very nearly, but on passing towards the tail the discrepancy between the two increases. The sensory area lies relatively further tailwards than the corresponding muscles.† The cutaneous nerves in passing to the skin take a more and more oblique direction the further tailwards their origin.‡ In the tadpole those nerves which run to the tip of the tail arise not far from its base and pass nearly longitudinally to their destination.

The shifting of the epidermis during development over the subjacent muscle plates, as ascertained above experimentally, corresponds in direction and in relative amount in the different regions with the displacement of the sensory area as compared with the motor belt of the same segmental nerve. In the region of the upper dorsal vertebrae there is but little shifting and but a slight segmental discrepancy between sensory and motor zones, while both increase gradually as the tail is approached.§

Wandering of skin, then, like wandering of muscles, occurs during development, but the nerves remain to indicate the course of this ontogenetic wandering of the one as well as of the other.

These considerations suggest that a connection between each ganglion cell and its end organs in the integument is established early in development, and that each nerve rudiment in its first stage passes from its origin in the ganglion cell by the shortest path to the integument; and conversely, that each portion of the integument in this stage is innervated by that nerve the root of which has its origin nearest to it. The more complicated relations found in the adult are due to the gradual drawing out of these connecting nerves, as the parts separate during development.*

There is indication that in each region where there is discrepancy between sensory and motor zones, the cause of the shifting is to be sought in the actual pulling of the skin, which results from the unequal growth of subjacent structures in the embryo. Thus, in man the rapid growth of the hind limbs would have the same effect as that of the tail of the tadpole in pulling the skin from above. Likewise, it does not seem improbable that the great increase in the size of the brain may account in the same way for the distribution of cervical nerves to the occipital region.

Of course it is meant to explain in this way only the course of the main nerves and not the finer anastomoses, and it is not intended to deny that other factors than the shifting of the skin play a part in determining the course taken by its nerves in the adult. For instance, this must certainly be the case with the lateral branch of the vagus; for the sense organs of the lateral line in the grafted larvae just described form a complete series extending to the extreme tip of the tail and continuing without break or bend from the integument of one component to that of the other, although, as can be directly observed, all of them receive fibres from the ramus lateralis vagi, which are derived entirely from ganglion cells of the anterior component. This must mean that in this case a connection is established secondarily between these ganglion cells and the sensory cells in the epidermis of the transplanted piece. This probably takes place in the same manner as a severed nerve grows out again to its end organ.

III. The Regeneration of the Tail.

For the purpose of controlling the experiments described in

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* This supports H. Virchow's (23) conclusion drawn from the study of the formation of the tail in Elasmobranchs.

† This has been shown physiologically most recently by Sherrington (22) who has worked the matter out especially carefully on the monkey, Macacus, giving a full account of previous work upon the subject. Unfortunately, in the frog, his study was confined to the hind limbs alone and did not include the trunk. In man the sensory areas have been very completely defined, clinically, by Head (7) whose diagrams show very clearly the increasing discrepancy between the level of the exit of the nerve from the vertebral canal and its area of distribution in the skin, as the sacral region is approached. As Sherrington points out, there is more than a general correspondence between his own results and those of Head.

‡ This is independent of the oblique course taken by the nerves in passing from the origin in the cord to those points of exit from the vertebral canal, which is accounted for by the unequal growth of the spinal cord and vertebral column.

§ When the position of the sensory area is compared with the point of origin of the nerve from the spinal cord, the segmental difference between the two becomes even more marked. And this difference affords a much more exact measure of the amount of shifting of the skin, since, as shown above, the muscle plates shift considerably in the same direction during development.

* This conclusion is identical in part with the well known view of Hensen (8, page 121), "dass die Nerven nicht ins Gewebe hineinwachsen, sondern durch die allmähliche Entfernung der einzelnen Zellen und Gewebe von einander ausgezogen würden." But it cannot be said to lend positive support to the opinion expressed less reservedly in a later paper (Hensen, 9, page 373), "dass die Nerven niemals ihrem Ende zuwachsen, sondern stets mit demselben verbunden sind." Nor do the observations above described offer any evidence as to exactly how and when the connection between nerve cell and end organ arises. They are, therefore, not to be construed as necessarily contradicting the view, at present almost generally accepted, that each axis cylinder grows out centrifugally from the ganglion cell to the end organ.

the second and fourth sections the normal regeneration of the tail was studied. The following account based upon this study refers almost exclusively to the regeneration of the peripheral nervous system, concerning which some new observations are recorded. These, while supplementing our meagre knowledge of this subject, are still of a preliminary nature.*

The material used consisted of larvae of R. palustris and R. virescens in three different stages of development. All of these are much earlier than those studied by previous writers. The youngest stage is the same as that used for the transplantation experiments (Fig. 2). The next stage is represented by larvae two days older (6.5 mm. long) and the third by those six days older than the first (9 mm. long). On account of the absorption of the greater part of the yolk having taken place in the last named, these were found to be the most favorable for histological study, and it is upon these that the description is largely based. Serial sections, best cut parallel to the frontal plane, were found to be indispensable.

The regularity with which the tail is regenerated is remarkable although, even in outward appearance, the regenerated appendage (Figs. 2 and 4, Pl. X) never becomes exactly like the original (Figs. 1 and 3, Pl. X). In the former the series of muscle plates does not taper quite so gradually to the end, and there is an absence of that slight thickening in the axial muscles which marks the middle region of all normal tails. Besides, the regenerated tails are much more heavily pigmented than the ones which they have replaced, and in R. virescens there are three or four blotches of black pigment arranged in a row along the lateral line which are not found in the original tails (Fig. 2, Pl. X).

The changes which mark the beginning of the rehabilitation of the peripheral nervous system of the tail may be observed within the first twenty-four hours after amputation.†

In a specimen preserved eighteen hours after amputation, which is the earliest stage examined, a few fine nerve fibrils are seen to pass out from each side of the spinal cord at a point very near to the cut end. These arise from cells within the cord and have been regenerated since the operation. They are distinct from the fibres which comprise the last nerve root arising from the old part of the cord. The ganglion of this nerve was removed in the operation, but the fibres of the motor root are seen to pass obliquely outwards and backwards. In later stages they mingle with the fibres regenerated from the cut end of the cord.

In a specimen preserved forty-three hours after amputation the new nerve is very well marked, and contains a very considerable number of fibres. The spinal cord is entirely closed in and now extends 0.2 mm. beyond the origin of the nerve, indicating new growth to that amount. At the root of the nerve and extending both proximally and distally within the substance of the cord there are situated a number of ganglion cells, which are still but slightly differentiated. It is from these cells that the nerve fibres, at least in part, arise. The new nerve is joined by a number of fibres from the next nerve root, which is the last one arising from the old part of the cord and from which the ganglion was cut off. Likewise this is connected with the last of the remaining ganglia by means of a longitudinal commissure.* And in this particular case, upon which the description is based, though not in all others, an anastomosis exists between the newly regenerated nerve and the n. lateralis vagi which passes along the lateral line close by.

After the new nerve trunk is formed, as later stages show, many of the ganglion cells which were situated at the root of the nerve wander out from the cord and form a large peripheral ganglion.† In some cases a chain of ganglion cells extends from the last ganglion of the old part of the tail to the new ganglion, so that some of the cells of the latter may possibly be derived from the persisting ganglia. In other cases this is not true, and in all cases observed the majority of the cells of the new ganglion are traceable directly to the cord. What is more remarkable, the cells which arise from the cord seem to come rather from its ventral side, although the cord is in this region so slender that a division into the dorsal and ventral zones of His can scarcely be made out. Even when the new ganglion is fully developed, a number of nerve cells still remain in the cord grouped around the point of exit of the nerve. These no doubt represent the motor elements, while those which wander out are the sensory cells.

The essentials of this new development of the peripheral nervous system take place within the first five days after the removal of the old appendage. At the end of this time the new nerve may be followed for some distance peripherally, where it seems to end in close proximity to the regenerating muscle cells.

In tails which have regenerated five days or more a few ganglion cells may usually be found scattered along the new peripheral nerve trunk. Later these cells segregate into several groups. In a specimen regenerated ten days two such groups of cells were found, and the diminished size of the original regenerated ganglion indicated that migration of cells from there had taken place. This may be interpreted as an attempt to restore the more distally situated ganglia which were removed in amputation.

The study of much older stages shows, however, that the lost ganglia are never entirely restored. In a case where the tail had regenerated for over two months no nerve cells are to be found in the new portion of the tail beyond the original regenerated ganglion, which is situated opposite the twelfth myotome. This ganglion is large and from it several stout nerve trunks pass to the periphery, forming anastomoses with nerves arising further headwards.

In another specimen regenerated the same length of time two groups of ganglion cells were found on the regenerated

* Fraisse (6) and Barfurth (2), treating of the general subject of regeneration, devote much attention to the study of the amphibian tail. A full account here would therefore necessitate much repetition.

† In this respect the younger larvae here studied must differ markedly from the older ones, where, according to Barfurth, the peripheral nerves are the last structures to begin regeneration.

*Such longitudinal commissures connect all the nerve roots of the normal tail as was shown by Hensen (8).

†The presence of this ganglion has been noted by Barfurth (2, page. 428).

nerve, and in still another, three groups of cells were present. With the exception of but one case it has not been possible to demonstrate separate dorsal roots in connection with any of these secondary ganglia; nor, as far as could be observed, do any motor roots leave the cord at any point distal to the origin of the first regenerated nerve. At least, no noticeable nerve trunks do. Nevertheless, there are a considerable number of ganglion cells and nerve fibres in the regenerated part of the cord, so that some fibres may be given off from here at intervals, perhaps singly and sporadically.*

The difference between the innervation of the normal and of the regenerated tail is, however, not so great as might be assumed from the above account, for the ganglia of the normal tail extend by no means to the tip.† In R. palustris at least the distal half of the tail is destitute of spinal ganglia. The greater part of the tail fin is innervated by branches of the large nerve trunks which arise near the root of the tail, and which, forming a plexus, give off branches to the skin and muscles of the distal part.

In the lizard, according to Fraisse, no spinal ganglia are regenerated at all after amputation of the tail, and the regenerated part of the spinal cord remains in a rudimentary condition. The new tail is innervated by three pairs of stout nerve trunks which arise from the last segment of the uninjured part of the cord. The last ganglion as well as the roots of the nerve pair are much larger than usual.‡ In Pleurodeles the ganglia are regenerated from the ventral side of the spinal cord, while in Proteus ganglia of the tail which here extend to the tip, develop in the embryo in the same way.§

The condition found in the regenerated tails of anouran larvae (R. palustris and R. virescens) seems, therefore, to be intermediate between the conditions found in the Lacertilia and the Urodela. As compared with the regenerated tail of the lizard, that of the tadpole more nearly attains the condition found in the normal tail.

IV. Regeneration of Reversed Tails.

The study of regeneration shows that a lost appendage is reproduced in a manner much the same as the original mode of development. After amputation of the tadpole's tail a new one grows out which closely resembles the one cut off. The "polarity" of the organism is maintained. On the other hand, tails which have been severed from the body do not regenerate the lost trunk and head, as is true of almost any portion of such animals as planarians or hydroids, where the power of regeneration is well nigh perfect. Nevertheless, a tail removed from the body when yolk is present in its tissues, may live for ten days or more, and besides undergoing normal growth and differentiation, may show signs of beginning regeneration headwards.* It might, therefore, be urged that non-regeneration is due to lack of food supply. By the method of grafting it is possible to implant an amputated tail by its distal end into the body of another larva, and thereby supply it for an indefinite period with proper nourishment, so that its capacity for regeneration from the head-end may be tested under favorable conditions. These transplanted pieces may be placed in what is termed the reversed natural position that is, in place of the removed tail, or they may be grafted to any desired region of the body of another individual.

It is obvious that in the former case two like ends or "poles" are united together. The free head-end of the grafted stump is in the same position with regard to the whole organism as is the free tail-end of a larva from which the tail has been cut off. But a tail is necessary to complete the organism in the former as well as in the latter case. The question then arises, whether a tail will be produced under the influence of the position of the regenerating centre with regard to the whole organism, or whether the elements in the transplanted stump retain their original orientation and strive to reproduce the lost body.† By varying the position of the transplanted piece, as mentioned above, it is possible to test the influence of functional activity upon the regenerating parts.

A. Tails Grafted in Reversed Natural Position.

Owing to the small size of the tail-bud at the grafting period it is impossible to perform directly the experiment in which the tail is reversed. The double wound which would be necessary in order to do this is sufficient to cause the maceration of such a small piece. In order to avoid, therefore, two simultaneous cuts, the tail-buds of two larvae may be cut off and the larvae brought together end to end. After the expiration of a certain time (from one to six days) when the two individuals are firmly united and the tail stumps of each stand out more or less from the body, the two may be cut apart as shown in the sketch (Fig. 10). Thus a small part (as future development shows, portions of three or four myotomes) of the base of the tail of one larva is left attached to the tail-stump of the other, but obviously the two ends of the transplanted piece are reversed. That which was turned headwards when in connection with its own body now forms the free distal end of the tail of the new individual to which it is attached. After cutting apart, both larvae may be kept

* Cf. Hensen (8).

† This has been clearly demonstrated by Hensen (8) who has given an admirable description of the nerves of the tail. This has been supplemented more recently from the histogenetic side by von Kölliker (13).

‡ Fraisse, page 120.

§ Fraisse, page 123.

* Vulpian (25) and Born (3) have made a study of the life of such isolated tails. The latter records that both notochord and spinal cord show signs of regeneration headwards, and that they grow out to some extent into a kind of fin-fold formed by the growth of the epidermis out beyond the surface of the wound. The cut muscle fibres show signs of degeneration as is usual before the actual regeneration begins, although in these cases the process does not pass beyond the initial stages. A full account of Vulpian's work is given by Born (p. 378).

† This is analogous to Morgan's (17) experiment with earthworms. Wetzel (27) has also recently made a similar test with hydra (see foot-note p. 188).

under the same conditions and observed daily in order that the regenerative process in each may be compared.*

This experiment was made in a large number of cases. The results were, however, in a high degree variable, so that it will be necessary to describe a number of individual cases. It seems best to begin with the one in which regeneration took place most regularly, that is, in a manner most like the normal regeneration from the caudal end.

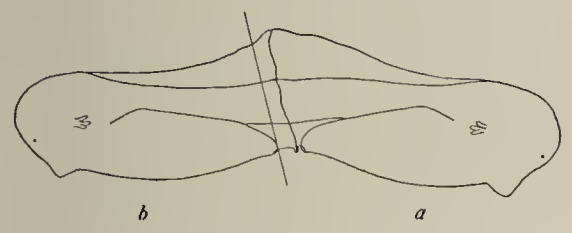


Fig. 10.

Case 1. Two days after operation, showing cut made to separate the two components. ×8.

Case 1.—Both components R. virescens. Cut apart two days after union (Fig. 10). On the day after cutting, the epidermis could be seen to extend a short distance beyond the axial structures as a result of the general backward shift-

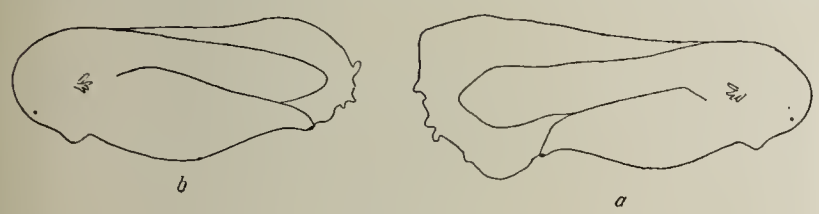


Fig. 11.

Case 1. Three days after cutting apart. *a*, combined larva; *b*, accessory larva. ×8.

ing of the whole layer. There is a slight swelling in the axial musculature where the tissues of the two constituents adjoin. Three days after cutting the epidermis has pushed out much further, and its periphery is still rough as in the initial stages of ordinary regeneration (Fig. 11, *a* and *b*). The axis of the tail tapers out to a point and there is already an increase of tissue at this growing end. The cells being still full of yolk granules, the larvae are so opaque that the exact lines of internal structures (myotomes, notochord, etc.) cannot be made out. Comparison of the two larvae shows similarity in the conformation of the tips of the tails.

On the sixth day enough yolk is absorbed from the tissues to render the tail more or less transparent, and now the blood may be seen for the first time circulating in the tail, in the transplanted stump as well as in the larva proper. The fin-fold has grown still further distally, and although there are still a number of surplus cells along its periphery, which give it a ragged appearance, its end is beginning to round off (Fig. 12). The transparency of the tissues now enables one to make

* Of course, in the strict sense, this comparison should be made between regenerating grafted tails placed in normal orientation, and regenerating reversed tails, but since it can be shown that the grafted tails regenerate as readily as original tails, this precaution does not seem necessary (page 190).

out the contours of the muscle-plates, which are by this time distinctly V-shaped. In those derived from the principal larva, the angle of the V-points, of course, away from the tip of the tail, but those of the transplanted piece are reversed. They are oriented just as they would have been had they never been removed from their original position. This characteristic

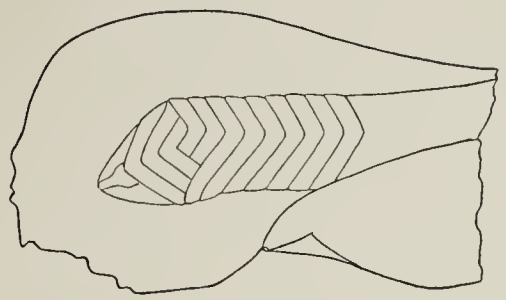


Fig. 12.

Case 1. Tail portion of combined larva (Fig. 10 *a*) five days after cutting apart. ×14.

shape of the muscle plates had been acquired, however, before the two larvae were cut apart, to some extent even before they were stuck together. The myotomes of the two constituents are dovetailed together. The notochord may also be clearly seen. It extends a short distance out beyond the original muscle-plates. Between the latter and the tip of the notochord there are numbers of undifferentiated sarcoblasts.

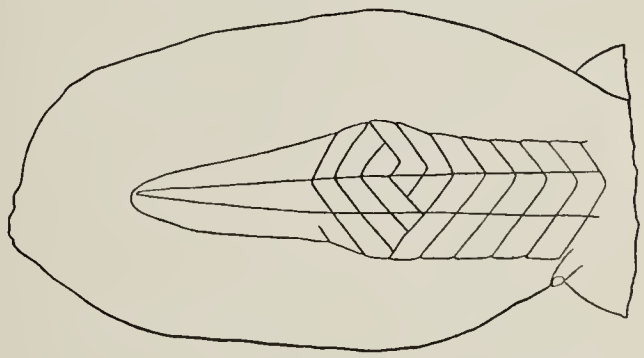


Fig 13.

Case 1. Nine days after cutting apart. ×14.

On the tenth day, still further advance in development is to be noted. The fin-fold is now well rounded off, and is beginning to become pointed as in the normal tail (Fig. 13). A slight aggregation of superfluous ectodermal cells makes a little thickening at the tip. The blood circulation is well established throughout the whole tail. The contours of the muscle-plates, where the tissues of the two constituents adjoin, are about the same as they were when first noted. Measurements show that the notochord has grown 1.5 mm. in the last four days. Differentiation in the regenerated portion is progressing. The more proximal of the sarcoblasts situated between the old myotomes and the tip of the notochord have given rise to muscle fibrils in which cross striation is plainly visible.

On the fifteenth day, the transplanted portion of the *chorda dorsalis* is over four millimetres in length. The tail now tapers gradually to a point, and can scarcely be distinguished from a normal tail except for the slight swelling of the

muscle-plates at the place where the two larvae were stuck together. Moreover, the creature is now very active, and swims as well and as rapidly as any other tadpole of its own size.

On the twenty-ninth day the transplanted portion of the notochord has attained a length of 7 mm. The whole length of the organism is 17.5 mm., of which 10 mm. is tail. The tail of the larva with which this was united is just 10 mm. long, although the body is somewhat longer, 8 mm. It is seen, therefore, that the normally regenerated tail has grown quite a little faster than the appendage regenerated from the head-end, for, at the start, the former was shorter than the latter by the length of about six myotomes. The reversed tail is slightly crooked. The tip, for instance, is bent over to the right side. This does not, however, interfere with the rapid locomotion of the animal.

This irregularity increased but little as time went on, as may be seen from comparing the two photographs (Fig. 14 and Fig. 15, Pl. X) taken respectively thirty-eight and eighty-nine days after the cutting of the larvae apart. The musculature is somewhat stouter than in an ordinary tail (Figs. 1 and 3, Pl. X) or even in a normally regenerated tail (Fig. 2, Pl. X). The whole appendage is not so long and the fin-fold is broader and more rounded at the tip. The notochord has evidently grown more rapidly than the other structures, and hence takes a wavy course from base to tip. The tail is also very heavily pigmented, and although all regenerated tails of R. virescens are darker than the normal, none were observed so dark as this and other reversed ones. The creature has grown on the whole more slowly than the average, and is inferior to its fellow in size, although it is very active and uses its tail to as much advantage as a normal individual. Stimulation of the extreme tip with the point of a sharp needle brings about the usual sudden reflex.

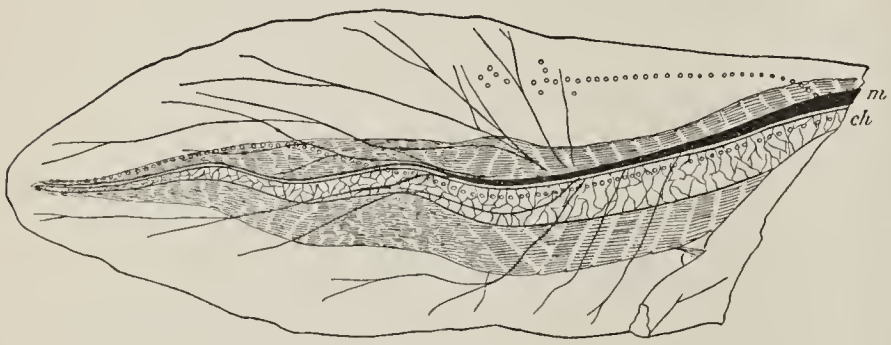


Fig. 14.

Case 1. Ninety-five days after cutting apart, as seen after staining and clearing. *m*, spinal cord; *ch*, notochord; *o o o*, sense organs of the lateral line. × 6.

A little over three months after grafting, this specimen was preserved for the purpose of more minute examination. After being stained and cleared, it was first studied *in toto* as a transparent object, and was cut afterwards into a series of frontal sections. The main features of the tail seen as a transparent object are shown in Fig. 14. The notochord passes continuously from the region of the principal larva out into the grafted tail. An examination of the sections shows beyond doubt that the chordal tissues of the two constituents are fused completely with one another. This is unusual, and no doubt accounts for the exceptional degree of perfection attained by the regenerated tail in this individual case. The contours of the original muscle-plates, although considerably obscured by pigment, may nevertheless be traced out, and are substantially the same as when first observed. The regenerated fibres do not form very definite muscle-plates, but are divided up into bundles which overlap more or less with each other. The individual fibres are somewhat shorter than those at the root of the tail. A vague tendency to regular arrangement may nevertheless be made out. In the proximal part of the regenerated tail this is less apparent, but distally there is a grouping of the bundles into fairly regular segments. The contour of those quasi-myotomes tends to correspond to that of the myotomes of normal tails. They are not reversed. The spinal cord extends out to the tip of the tail and follows closely the wavy curves of the notochord. The regenerated part contains few or no ganglion cells or nerve fibres, and seems to have remained in a still more rudimentary condition than the new growth of cord in normally regenerated tails. The peripheral nerves radiate from a region in the non-regenerated part of the tail, both from the region of the larva proper and of the reversed piece. A large ganglionated plexus is situated there, the nerve cells of which are probably derived from both constituents).* Thence the sensory nerve fibres pass to all parts of the fin-fold (see Case 3). Those which are destined for the extreme tip of the tail pass almost longitudinally between the muscle-plates of the two sides and emerge into the fin-fold well on towards their peripheral ends. One pair of nerves passes for some distance very close and parallel to the spinal cord, but in the regenerated part of the tail no nerves could with certainty be observed to arise directly from the cord.

The main series of sense organs of the lateral line has exactly the same position and distribution as usual. It extends along the side of the tail at the level of the notochord, following at first the bend of the latter. At the beginning of the distal half of the tail it passes gradually to the level of the dorsal edge of the muscle plates, along which line it extends as far as the tip of the notochord. The dorsal series of organs situated on the dorsal fin-fold are not so regular and do not extend so far peripherally as is the rule. Some interruption to their normal development must have occurred.

Case 2.—Both components R. virescens. Cut apart after being united six days. At the expiration of this time the yolk was for the greater part absorbed and the two larvae were quite active, struggling always in opposite directions. When cut apart in the same manner as in the previous case, blood streamed out from both larvae, showing that circulation had been established from one to the other.

Regeneration took place as in the Case 1, but perhaps not quite so typically. The tail was considerably more blunt (Fig. 17, Pl. X). Functionally, however, it was a very satisfactory organ; this larva was one of the most active of those experimented upon. The arrangement of the muscle fibres

* This is certainly true in a number of other cases, which were preserved and cut into sections at a much earlier stage of development.

and the general distribution of the peripheral nerves in the fin-fold is the same as in the first instance. This specimen was kept alive for eighty-two days. At the expiration of this time the hind legs had developed to a considerable extent, although they were by no means so far along as is usual at the time of metamorphosis. Nevertheless, signs of degeneration were beginning to manifest themselves at the tip of the tail in the form of shriveling of the fin-fold and the extremity of the axial structures (see page 189). The specimen was preserved before the atrophy of the grafted tissues was complete.

Case 3.—In this experiment the two constituents were stuck together in the same way as before, but one of them was a palustris larva, while the other was a virescens. After being united for two days they were cut apart as shown by the line in Fig. 15, the virescens larva being left with a small portion

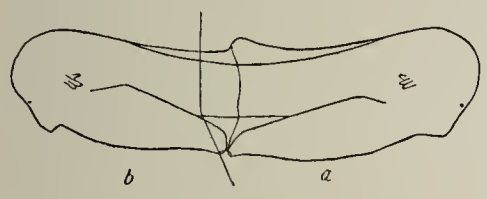


Fig. 15.

Case 3. *a* virescens, *b* palustris constituent, ×8.

of palustris tissue attached. It will be seen that a small bit of yolk, including the anal opening, was cut off along with the tail stump. At the time of cutting the epidermis of neither larva had encroached upon the other, the pressure from each end being presumably the same. Six days after this the epidermis of the virescens was seen to extend well out over the palustris tissue dorsally. The line of demarcation (Fig. 16) between the two extended from the tip of the tail

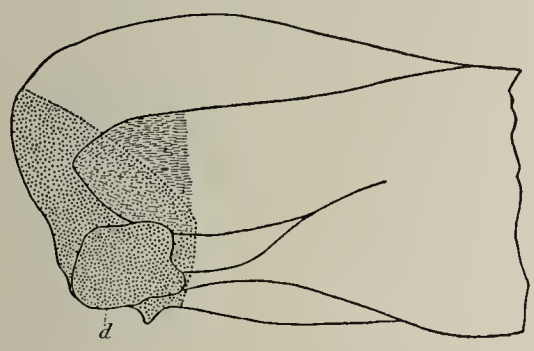


Fig. 16.

Case 3. Tail portion of virescens component (Fig. 15 *a*) six days after cutting apart. Stippled field, palustris epidermis; shaded field, palustris musculature; *d* palustris yolk. ×14.

ventrally and headwards until a little below the level of the notochord where it was seen to bend ventrally. Apparently the boundary had remained nearly fixed in its ventral portion, the movement being held in check by the two anal openings (cf. page 177). This shifting of the epidermis in the same direction as in normal growth helps to explain the course taken by the nerves in the first case described. The arrangement of the muscle plates presented about the same peculiarity as in the former cases. The mass of grafted yolk retained its position and on the sixth day was still but little differentiated. The end-gut of the principal larva seems to have been fastened to that of the grafted piece, for it was pulled out horizontally beyond the usual distance. This defect was corrected as development proceeded.

This specimen continued to thrive. Fifteen days after cutting the transplanted notochord had attained the length of 3 mm.,* the whole tail being about 5.5 mm. long. In view of the almost perfect regeneration of this tail it is highly probable that the two notochords were entirely fused (see page 463. It was able to swim actively, being hindered only to a slight extent by the presence of the small mass of endoderm attached to the tail. This marked the place of union of the two constitutents, and by this time was fully differentiated into a miniature coiled intestine, which was suspended by a mesentery in a small body cavity, and could be observed to undergo continual peristaltic movement. Blood could be seen circulating freely in the walls of the intestine and mesentery. Unfortunately, this larva died shortly after these last observations were made, and was not available for histological study.

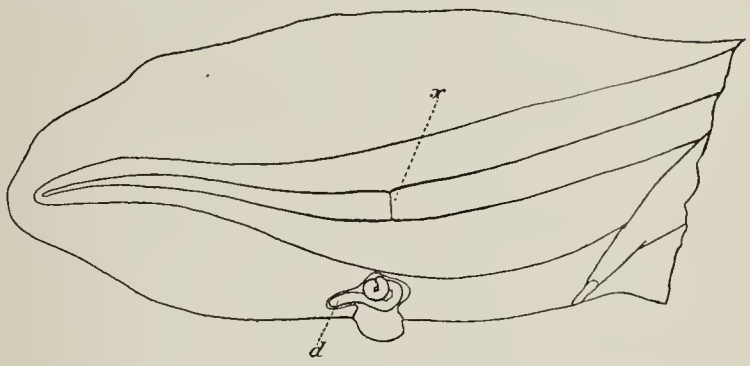


Fig. 17.

Case 3. Tail portion of *a* (Fig. 15) fifteen days after cutting apart; *d* intestine developed out of grafted yolk. ×14.

Sections were cut off several other specimens which had been treated in the same way. The intestine was found to contain a number of free cells, but of course no food matter. The anus was preserved intact and in one instance the rudiments of the hind legs, which had been removed with the piece of yolk, could be detected. These instances indicate the high degree of specialization of the tissues at the time of grafting even though it may not be always visible to the eye (see note, page 187).

Case 4.—In this case the two larve, both virescens, were cut apart three days after union. At this time the epidermis covering the wound had begun to show sighs of unevenness and crumpling. Two days after cutting apart a small hump made its appearance on the dorsal side of the muscle plates at the place where the two components were combined. This increased rapidly and formed a prominent projection, which on the twenty-sixth day had attained the length of 1.5 mm. The body of the larva had then attained a length of 7 mm. and the tail 8 mm. The notochord of the transplanted piece was but 2.5 mm. long as against 7 mm. in Case 1. The exter-

*I cannot be quite sure of the exact length of this because the place of union could not be made out in the living specimen, although there were indications of a line at × Fig. 17.

nal form of this specimen as it appeared forty-five days after the operation is shown in the photograph (Fig. 16, Pl. X). After being strained and cleared it was ascertained that the notochords of the two constituents had not united, but that their ends overlap somewhat and are bound together by connective tissue. At the point where the two spinal cords were joined together there is a vesicular enlargement, triangular as seen from the side in optical section. Extending from the apex of this triangle a short prolongation of the cord accompanies the dorsal prolongation of the muscle-plates mentioned above. In this case the two constituents were evidently not united so exactly as in Case 1, so that the tissues of the main larva had an opportunity to grow out. Correspondent to this there was a retardation of the distal growth of the grafted piece. The forked condition of the spinal cord is, however, a rather rare occurrence, and especially so in the absence of a forked notochord.

Case 5.—In this instance both constituents were R. palustris. In preparing the larvae for grafting the tails of both were amputated obliquely, so that when stuck together the axes of the two, instead of being in a straight line, met at an angle of about 135°. The two were kept united for six days, and at the expiration of this time it could be seen that the notochord of one had regenerated ventrally, having grown out into the ventral fin-fold. Accompanying this new growth of notochord were embryonic muscle-cells and blood-vessels, but no spinal cord. The two larvae were cut apart so that one whose chorda was regenerating was used as the principal larva, to which the inverted tail-stump of the other was left attached. This larva had, therefore, a forked tail from the start. The

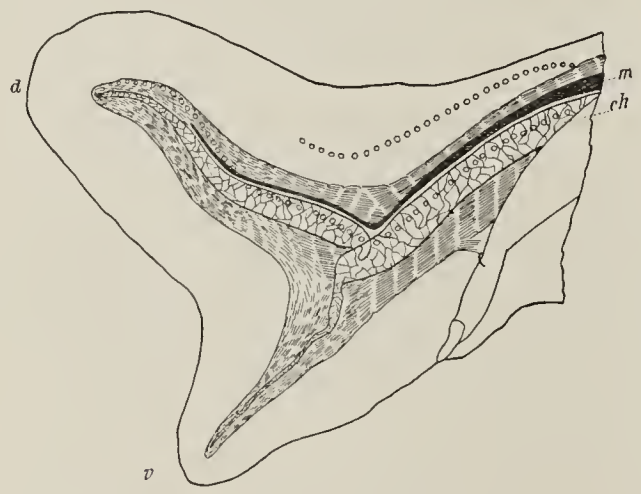


Fig. 18.

Case 5. Tail, preserved forty-five days after cutting apart; *d*, dorsal fork of tail supported by chorda of grafted piece; *v*, ventral fork of tail supported by regenerated chorda of chief component; *m*, spinal cord; *ch*, notochord; *o o o*, sense organs of lateral line. × 9½.

upper or principal fork was constituted by the transplanted reversed tail, including its notochord, muscle-plates and lastly its spinal cord, which was completely fused end to end with the spinal cord of the principal larva. The outgrowth from the tissues of the principal larva formed the ventral fork of the tail. Both of those branches grew and increased in length and so that shortly after the operation the tail bore a certain resemblance, entirely superficial of course, to the heterocercal tail of a shark (cf. Fig. 18, Pl. X, which is taken from another specimen treated in exactly the same way). After forty-five days had elapsed, this specimen was preserved and studied as a transparent object (Fig. 18). The notochords had not united. The outgrowth of the chorda forming the ventral fork is of a much smaller calibre than the original part, and presents a wavy or crumpled appearance. That of the transplanted piece is almost normal, but is slightly wavy and ends rather bluntly. It has a length of about 4 mm. Its proximal end is not united to the chorda of the main component, but is bent around ventrally to the side of the latter. The muscle-plates are differentiated as usual. The original ones in the transplanted piece are reversed, while the newly regenerated muscles of this fork present the usual irregularity. This is likewise true of the muscles of the ventral fork, which are undoubtedly derived from cells from both constituents. The fibres of this fork bend around and are continuous with the axial fibres both orally and caudally. The sense organs of the lateral line are continuous out along the dorsal fork, that is from one constituent to the other. The series does not divide, there being none along the ventral fork.

The forked tail in this instance was due no doubt to the fact that the notochords of the two larvae did not abut against each other, thus allowing one the freedom to regenerate. The chance to react in this way was increased by the fact that the axes of the two tails made a considerable angle with each other. This effect is not always the result of these conditions, however, and besides a forked tail may be formed when the two axes are united in a straight line. The length of time during which the two larvae were united is not a factor to be considered in this connection, since in a majority of cases in which the two were united for six days, simple tails resulted, and forked tails were found in several instances where the two larvae were united for but a single day. The irregularities probably arise before the two components are cut apart.

Case 6. A palustris larva was united to a virescens. The two were cut apart on the third day, leaving a small portion of the virescens attached to the palustris. A ventral outgrowth was formed, but in the present case it originated from the transplanted piece and not from the chief constituent as in the previous. The notochord bent around at almost a right angle, and embryonic muscle-cells derived from both constituents accompanied the growth of the chorda. The spinal cord took part likewise and became forked; this is rather exceptional. The organs of the lateral line were present in both forks. In this case, therefore, both forks were derived from the transplanted piece, and we had here the tissues of this piece growing and regenerating from both ends simultaneously, but the resultant tail was not as efficient an organ functionally as any of the cases described above. There is no essential difference in the origin of the irregularity in this case and in the last, for in both the regeneration had undoubtedly begun before the larvae were cut apart. The difference lies in the manner of cutting apart, but it is only in the present instance that we have one and the same notochord regenerating from both ends.

Case 7. Both constituents were R. palustris, and were cut

apart the day after they were united. On the twenty-third day after cutting apart the specimen was killed. At this time the tail had attained a length of 5 mm. The regenerated part was 4 mm. long and was regenerated from the tail of the principal larva, being very nearly straight and normal. The transplanted piece formed but an insignificant hump on the left side of the dorsal fin-fold, and was attached to the muscle-plates on the dorsal side. Neither the notochord nor the spinal cord was fused with the corresponding structures of the principal. No appearances of regeneration were present in either.

The following summary is an attempt to classify the various forms resulting from the same operation as described above. The frequency of each is also given:

I. Simple tails were regenerated from the cranial pole of the transplanted piece. Twenty-six instances.

a) The notochords of the two constituents were completely fused. Two instances (possibly three).

b) The notochords were partially fused. Two instances.

c) The muscle-plates and spinal chords respectively, were fused, but the ends of the notochords merely abutted against each other and were united by connective tissue, the resulting regenerated tail being less perfect than in a). Twenty-two instances.

II. Double regeneration took place, resulting in forked tails. Ten instances.

a) This was due to the regeneration of the notochord and muscle-plates of the principal constituent. Five instances.

b) This was due to the growth of the tissues of the transplanted piece from both ends. Two instances.

c) Both nerve-cord and notochord were forked. Two instances.

d) Nerve-cord alone was forked. One instance.

III. No perceptible regeneration of any kind took place. Three instances.

IV. Regeneration took place in the tissues of the principal constituent alone. The grafted piece, which was but imperfectly united in the first place, remained as an insignificant mass at the side of the newly regenerated tail. Seven instances.

B. Tail Grafted to Various Parts of the Body.

Case 8. A small piece (including yolk as well as integument) was cut out of the ventrolateral body-wall of one larva, while the tail-bud was removed from another, and the two were stuck together by the cut surfaces. Both were larvae of R. palustris. They were cut apart after three days (Fig. 19). A week later the tip of the reversed tail had rounded itself off and a considerable amount of regeneration had taken place. Connection was established with the circulatory system of the principal larva, and a lively circulation was going on in the transplanted piece. This specimen was preserved on the twentieth day after cutting. The regenerated part of the reversed tail was a little over 2 mm. long. Both notochord and muscles with a well marked fin-fold had regenerated, but the spinal cord had not (Fig. 20). The mode of

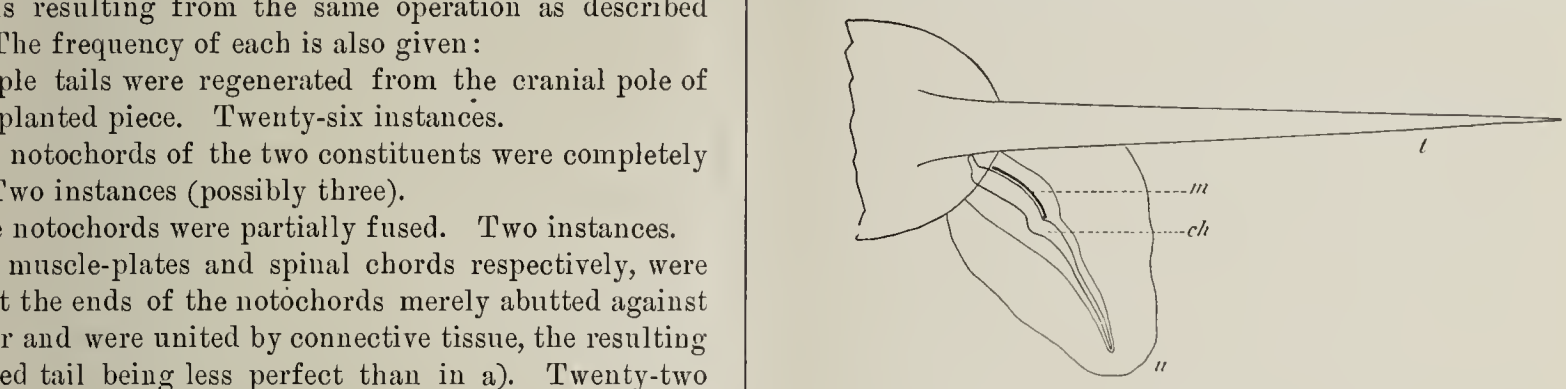


Fig. 19.

Case 8. Three days after operation, showing cut made in separating the constituents. ×8.

Fig. 20.

Case 8. Tail portion of Fig. 19 *a*. Thirteen days after cutting apart. *t*, tail of principal; *u*, regenerated tail-like structure; *ch*, notochord; *m*, medullary cord. ×8.

innervation of the grafted tissue could not be made out with certainty. Numerous sense organs, like those of the lateral line, but rudimentary and irregularly arranged, were present in the epidermis, but no nerves could be traced running to them.

Case 9. Operation was the same as in case 8, except that the two were cut apart after one day. The regeneration was not quite so regular in this instance, and the nerve-cord of the grafted tissue seems to have contracted or atrophied partially instead of having regenerated. There was, of course, no connection between it and the cord of the principal larva.

Case 10. A small cut was made in the dorsal fin-fold and muscle-plates of the body of one larva, extending about to the level of the spinal cord. The tail was removed from another and the two united. They were cut apart after four days, so that the reversed tail was left sticking to the back of the other larva. This grafted piece began to regenerate from both ends, the caudal end bending around so as to grow out freely instead of into the substance of the principal larva. Considerable growth took place from each end, but more from the oral than from the caudal (Fig. 19, Pl. X). This specimen was preserved after the expiration of four months and a half. It could be seen in the cleared object that only the muscles and notochord of the grafted tissue had regenerated. The nerve-cord had not. Large cutaneous nerves extended from the principal larva out into the regenerated part of the transplanted piece.

In a few cases tail-buds, not reversed, were transplanted to other parts of the body. Unfortunately, but two of these (Cases 11 and 12) were successful. In both of these the

supernumerary tail was fastened in the midline of the back of the other larva. In both cases the supernumerary tail grew and differentiated at first, but in neither was it ever used in swimming, although it was sensitive to stimuli. After a time atrophy ensued in one (Case 11) and the unused appendage was partially resorbed (Fig. 22, Pl. X). In the other (Case 12) the extra tail retained its normal form much longer (Fig. 21, Pl. X), although microscopic examination of the hardened specimen (preserved three months and a half after the operation) showed that both medullary cord and muscle-plates were involved in atrophy. The peripheral nerves, for the great part at least, originated from the principal larva.*

Discussion of the Material.

Complete as is the union in the great majority of instances between the muscle-plates and spinal cords respectively of the two components, perfect fusion of the notochordal tissues was found in but two cases, and possibly in a third. It was in these instances that the regeneration of the reversed part took place in most perfect form and almost as rapidly as regeneration from the caudal end. Where only partial fusion of the notochords occurs, which was observed in three cases, there may be considerable irregularity in regeneration. In one ef these specimens there was an actual branching of the chorda to one side.

In the great majority of cases there is no actual fusion.† The notochords of the two components are merely bound together by their connective tissue sheaths. In many such instances regeneration from either of the approximated ends is prevented, but a new growth is provided for at the distal end of the transplanted piece, though it does not take place quite so quickly nor is it so complete as when the notochordal tissue of the two constituents is completely fused. The organ which results in these cases, even if the nerve-cords and muscle-plates respectively be united, is less perfect than the tail described in Case 1.

It often happens that the two notochords do not abut fairly against each other, or are so loosely bound together that one of them has the opportunity to regenerate. This begins before the two components are cut apart, and continues after cutting, no matter whether the regenerating chorda belongs to the main larva or to the grafted piece. Since the grafted chorda grows from its present distal end also, a forked appendage results, the two forks being usually in the same sagittal plane, at least in cases where the muscle-plates are properly fused. In such cases the new outgrowth of chorda is always accompanied by muscle tissue, blood-vessels and by some nerves, but usually not by the spinal cord. The two portions of the latter unite so readily and exactly that there is but little chance for budding of the chord to take place from the region where the two components are joined. Such a bifurcation, however, occurred in some instances, three in all, and in one of these there was no forked notochord to support the secondary outgrowth. It is possible that the collection of cerebro-spinal fluid at the point where the two components are joined may give the first impulse to the outgrowth which results in the branch.*

If the union of the two components is so imperfect that neither the notochords nor the spinal cords are fused, and especially if the displacement be from side to side so that the corresponding muscle-plates do not join, then the tissues of the principal larva, being free to grow, begin to regenerate rapidly and soon outstrip the feeble growth from the distal end of the transplanted piece.† A new complete tail is thus formed from the principal larva; the grafted piece ceases to grow and remains as a hump on the side of the new tail.

When a reversed tail is healed to another part of the body of another larva, considerable regeneration takes place in both muscles and notochord. A tail-like organ is produced with a well-developed fin which is rounded at the end, but which is crumpled more or less. The spinal cord in these cases does not grow, however, and indeed it may be said that in all cases where the grafted cord remains isolated from that of the principal, it persists in a rudimentary condition or may even almost entirely degenerate.

These experiments establish beyond a doubt the fact that the regenerative power of the tissues of the tail is very considerable in both directions. The appearances of regeneration observed by Born in the oral ends of isolated tails are the mere beginning of what is possible, provided that sufficient nutrition is supplied and functional activity afforded. That the latter is an important factor, is shown by the contrast between reversed tails implanted in the natural position and those attached to parts of the body, such as the abdominal wall, the back or the side of the tail, as in Case 7, where they may only remain passive.‡

*In a case which Born described, a tail transplanted to the ventral body-wall disappeared down to a small stump in the course of time. In my attempt to repeat this operation I was unsuccessful.

†This has already been observed and commented upon by Born (page 394), who calls attention to the relative rigidity of the chorda even in early stages, and to the fact that the cut ends often project beyond the surface of the cut, as probable factors in preventing direct union. It may also be mentioned that there is but a relatively small quantity of yolk in the notochord at this time, and that it is by far the most highly differentiated of the tissues of such young embryos.

* These cases of forked tails are analogous (the ends being reversed) to those found in some instances by Joest (12) when the tail pieces of two earthworms were joined together by their oral poles. In seven such cases Joest found that heads regenerated at the place of union. In six of these but one head was formed, while in the seventh two were regenerated (l. c., page 488). Similarly in Hydra, Wetzel (26) found that when two decapitated individuals were joined together by their oral ends, mouth and tentacles were formed at the place of union and the two individuals ultimately separated.

†Born (page 396) records a case in which the muscle-plates of the left side of the anterior component pass continuously into those of the right side of the posterior component. I have found several similar cases in the above series.

‡Of interest in this connection are the experiments of Barfurth (1) bearing upon the functional adaptation of regenerating parts. The tails of a number of tadpoles were amputated obliquely. The axis of the regenerated tail, which is at first perpendicular to the plane of the cut, righted itself in time in all cases, but in those individuals which were permitted to swim actively, this adjustment took place much more quickly than in those subjected to enforced quiet.

In the intestine the regenerative capacity is but slight in either direction, but the power of self-differentiation is exceedingly well marked. This is shown in the persistence of small masses of endoderm which were cut off along with the reversed tail-stumps in several instances. These bits of yolk not only maintain their individuality for weeks, but also differentiate into miniature intestines with mesentery, blood supply and surrounding body-cavity; and this, even though functional activity is entirely excluded.*

As far as the histogenetic processes are concerned, there is but little difference between the mode of regeneration from the cranial and the caudal ends. For the purpose of investigating this matter a number of regenerating reversed tails were cut into serial sections.

The growth and histological differentiation of the notochord takes place just as in normal cases, beginning as a solid outgrowth of closely packed cells, which form a rod much more slender than the old chorda. Vacuolization of these cells takes place later.

The spinal cord rounds over the cut end. On the side of this, groups of ganglion-cells make their appearance, and from there a pair of regenerated nerves eventually passes to the periphery. Subsequently some of the ganglion-cells move out along the nerve-root (see p. 179). These processes take place considerably more slowly than when the regeneration goes on from the caudal end, and of course irregularities often arise.

The muscle-fibres which were injured in cutting the two larvae apart begin to break up, and traces of disintegrated fibrils may be found for four or five days. At the end of this time a layer of embryonic muscle-cells (sarcoblasts) extends from the uninjured myotomes to the tip of the newly regenerated notocord. Thus far the process is just as it takes place in ordinary regeneration. When fibrils are differentiated, however, the bundles do not become arranged into distinct muscle-plates (cf. page 182), but are more or less irregular (Fig. 14), while in tails regenerated from the caudal pole the arrangement of the muscle fibres assumes the same form as in the primary appendage. Obviously, there are several disturbing elements which bring the irregularity about. The muscle-plates directly adjacent to the newly regenerating muscles are reversed, and their contours must have some influence upon the arrangement of the newly differentiated fibres. On the other hand, the position of the latter as regards the tail as a whole is the usual one. The result is what might possibly be termed a compromise. The new groups of muscle-fibres become arranged neither according to their original orientation nor according to their new position with respect to the whole organism. There is a tendency, however, vague as it may be, for the more distally placed fibres, that is, those considerably removed from the influences of the old muscle-plates, to be arranged into quasi-myotomes with the angle of the V pointing forwards as in the usual form; but the explanation of this cannot be made clear until it is understood why the myotomes have this V-shape in all Ichthyopsida.

The question stated at the beginning of this section (page 180) now comes up for consideration. Are these cases to be regarded as examples of heteromorphosis, or not? Especially regarding such cases as Case 1, one is at first inclined to answer this question in the affirmative. In place of a trunk and head, which have been removed, there arises a tail-like appendage, which is an organ both structurally and functionally different. Loeb's definition is apparently complied with.* Regeneration from the original caudal end of the tail-stump was prevented by implanting that end into the tissues of another individual. The surrounding conditions of the two ends of the grafted piece are reversed and the outcome is much the same as in the case of Tubularia,† where sticking the oral end of a bare stem into sand prevents a polyp from being formed there, while the aboral end, being free to grow, does produce a hydranth. In the case of the reversed tail the said change of surrounding conditions consists in a change of relation with regard to the rest of the organism. We would thus have a case of heteromorphosis, brought about through functional adaptation to the needs of the organism as a whole.

But on closer examination a simpler interpretation of the phenomenon becomes possible. An inquiry into the grounds for calling the regenerated appendage a tail shows that while there is a striking resemblance in external form and in the arrangement of the various component parts, this similarity may be explained by taking into account the details of the regenerative processes. The notochord is merely a straight rod, lacking visible differentiation of its elements in a cranio-caudal direction; it is, therefore, not remarkable that its growth, whether proceeding from one end or the other, should take place in the same manner and give the same results. Much the same might be said of the blood-vessels. The spinal cord of the tail is in any case a rudimentary organ. The course of the peripheral nerves is explained by the shifting of the epidermis known to take place during development. In the only tissue in which there is normally a plainly visible orientation of the elements, viz., the axial musculature, the arrangement of the fibre bundles in the reversed tail is not as in a normal tail, either primary or regenerated, but is irregular. Moreover, when it is considered that the tail of a tadpole differs from the trunk in the absence of certain characters, and only to a small extent in the presence of distinguishing ones, such as the fin-folds, it becomes apparent that the tail-like organ above described is not much more than what might be called an imperfectly regenerated trunk.

Thus the cases under discussion, even such as Case 1 and Case 3, lose much of their significance as examples of heteromorphosis. At most they might be regarded as heteromorphic appearances by virtue of purely negative characters, but

* Born brings forward many facts which indicate the high power of self-differentiation in the tissues of frog embryos at the period when grafting is performed. He concludes (page 613): "Die Entwickelung entspricht also von unserem Ausgangsstadium an durchaus der Mosaiktheorie Roux's; die organbildenden Keimbezirke sind ausgetheilt (His)."

* Loeb (14) who proposed the term heteromorphosis defines it (page 10): "Die Erscheinung, dass bei einem Thier an der Stelle eines Organs ein nach Form und Lebenserscheinungen typisch anderes Organ wächst."

† Loeb, page 12.

better and simpler is it to call the phenomenon incomplete regeneration.

This interpretation is strongly supported by the second series of experiments, in which reversed tail-stumps were implanted to various parts of the body (Cases 8–10). Even in these instances a by no means inconsiderable amount of regeneration occurs, and the structure produced is not unlike a tail, for it possesses all the constituents of such, including well marked fin-folds;* and this takes place, although the possibility of functional adaptation to the purpose of locomotion is eliminated, and no tail is necessary to complete the organism. The effect which the position of the regenerating appendage produces is merely difference in degree of perfection. The more perfect appendage is produced when all of the constituent parts (chorda, musculature and spinal cord) of the transplanted piece are in union with the corresponding parts of the main component, i. e., are in quasi natural relations, so that they may enter upon the ordinary exercise of their function in co-ordination with the organism as a whole.

While it must be recognized, therefore, that functional activity is an important factor in regeneration, as indeed, for the ordinary welfare of a part already developed, it is of importance only to the extent that it brings about a higher degree of efficiency in the structure already capable of considerable independent development in a given direction, regardless of surrounding conditions. The present experiments do not justify us, however, in going further, in the conclusion that unusual relations imposed upon a regenerating part call forth out of material which would normally be used otherwise, an entirely new heteromorphic structure, as a functional adaptation to new surroundings, or as the result of a striving to complete the mutilated organism.†

Coupled with the occurrence of heteromorphosis is the question of the polarity of the organism. Unfortunately, the term "polarity" is used with many different shades of meaning. Fundamentally a purely geometrical conception, it signifies more when used by the morphologist, implying not only symmetry, but also an internal cause for that symmetry, by virtue of which every particle of the organism has the same polar relations as the whole. This conception is based upon facts gathered from the study of regeneration, which show that the smallest possible part of an organism capable of regeneration maintains the same orientation as the whole, from which it was cut. For example, in Hydra, a head regenerates from the oral end of a fragment, and a foot from the aboral end, when the fragment is left under ordinary conditions.*

By imposing various external conditions upon regenerating organisms the polar relations may be modified, but it seems scarcely justifiable to conclude that such facts do away with the polarity of the organism concerned; certainly, no more so than to maintain that the fact that the poles of a magnet may be reversed by the influence of a more powerful magnetic force, does away with the polarity of the magnet.

Nevertheless, it is perhaps unfortunate that the word "polarity" should be used in connection with the living substance, for in that case one involuntarily assumes the occurrence of phenomena of attraction and repulsion with protoplasm as the basis. At least as far as animals are concerned there is no indisputable evidence in favor of this assumption. Obviously, it may be tested best by means of grafting, whereby tissues differently oriented may be brought into organic

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* Only the spinal cord fails to regenerate, but this is always the case when the grafted portion fails to unite with the central nervous system of the main component.

† Analogous experiments upon other animals give likewise no firm support to the view that heteromorphosis may be brought about through functional adaptation. Morgan's (17) experiments upon earthworms (Allolobophora fœtida) give, as far as they go, a negative answer. In the experiments in question the posterior portions of two worms were sewed together; from one of these the tail was amputated. In all cases where regeneration took place tails were formed, i. e., the part which was cut off, not the part necessary to complete the organism and render it capable of further existence.

Wetzel (27) has made similar experiments upon Hydra. He united the oral portion of two polyps by the aboral end, and thus obtained a double individual; one head was afterwards cut off and in place of this a foot regenerated (page 71). This result is the opposite of Morgan's. Wetzel interprets this as a case of heteromorphosis (page 83), but in view of the small number of instances in which such results were observed, he is not willing to ascribe its occurrence to the influence of the uncut component upon the regenerating one. But even against regarding the case in question as heteromorphosis at all, there are objections, for it is not impossible that during the time elapsed between amputation and regeneration the whole of the mutilated component may have been absorbed down to the aboral end of the other component, from which, then, the foot might have been produced in the normal way (cf. Nussbaum, 20, page 12). Unfortunately, Wetzel records in his paper no observations controlling this possibility. Should this objection prove to be unfounded, it still remains that the sole positive character which serves as a basis for calling the phenomenon heteromorphosis, viz., the presence of gland cells in the newly formed foot, is by no means a good criterion. The difference between the gland cells and the epithelio-muscle-cells is only one of degree. Nussbaum (19, page 278) has shown that all of the epithelio-muscle-cells contain secretory granules, the gland-cells of the foot simply containing more. And further, in buds, transitional stages between the two kinds of cells are found at the place where the new foot is to be formed, i. e., muscle-cells are here directly transformed into gland cells in the course of ordinary budding.

* This is expressed more clearly and categorically in the oft quoted words of Nussbaum (19) as follows: "Auszerdem müssen wir zur Erklärung der Erscheinungen bei unseren Versuchen noch die Annahme machen, dass die Zellen wie in den Funktionen auch in der Struktur, in dem Aufbau ihrer kleinsten Theile hoch differenzirt seien, dass nämlich innen und auszen, vorn und hinten nicht allein an dem ganzen Individuum ihre volle Geltung haben, sondern dass die axialen Orientirungen des Individuums in den Orientirungen seiner kleinsten Theile begründet seien. Es muss also in jeder Zelle ein Vorn und Hinten, ein Innen und Auszen geben, rechts und links sind dadurch von selbst bestimmt . . . und da jede Zelle weiterhin theilbar gedacht werden muss, diese axiale Orientirung auch an den kleinsten Theilen der Zellen schon vorhanden sein" (page 348). As is also seen from a later publication, Nussbaum (20) intends the above to apply only to cells already differentiated.

continuity.* Even then, disturbances arising in such unions may be due to a variety of causes, such as the reversal of structural relations upon which the exercise of normal functions are dependent,† and are not to be compared off-hand with the repulsion of like poles of magnets. Thus, the irregularities resulting in the reversed-tail experiments, where two caudal poles are placed in juxtaposition, may be traced to the circumstance that two regenerative centres are brought together.‡

The only phenomenon which might be interpreted as the expression of some general organic disturbance resulting from abnormal polar relations, is the degeneration which set in in some of the reversed tails, as in Case 3. Also in Case 1, where the tail regenerated from the cranial pole was so perfect, indications of degeneration could be made out which involved both epidermis and the axial musculature. But no conclusion can be drawn from these in the absence of careful controlling experiments. Even should it turn out that the degeneration were due to abnormal position of parts, it could not be shown that there is any resemblance to magnetic repulsion.§

V. Reactions between Tissues Derived from Different Species.

Partly as a result of the experiments described in the second section, there were obtained a number of larvae of normal external form, but which were composed of parts derived from two distinct species. Many of these were kept under regular observation for a considerable length of time, in some cases for three or four months after the absorption of the food yolk.* The general biological interest attaching to such heteroplastic combinations is naturally great. The reactions between the tissues of distinct species, when united into one organism, deserve careful study. Unfortunately, the present material is far from adequate, but certain observations were made which seem to be of importance. These are here recorded in the hope that they may be supplemented at no late date.

First to be considered are those larvae in which the tail-bud alone was transplanted. In this combination the tissues of the one species greatly preponderate over those of the other. The grafting of the tail by itself is such a light operation (succeeding in about four cases out of five) that few abnormalities ever result therefrom. The larvae, at least at first, are perfectly normal and are as healthy and as active as any which are born in freedom and not experimented upon. The usual development of blood-vessels takes place in the tail, with the subsequent incorporation of these into the general circulatory system of the individual. The blood begins in time to flow freely from the body to the tail and back again to the body. Both parts are at first equally well nourished and grow commensurately, so that the usual aspect of the tadpole is not changed (Fig. 6, Pl. X). The body-constituent does not immediately cast off the transplanted tail and regenerate a new tail of its own species, but the latter persists even though it is of a different species, and affords a perfect substitute for the one replaced.† The tail preserves, moreover, in a general way, its specific characters even after months have elapsed, so that one who is familiar with the markings of the respective species would have no difficulty whatever in distinguishing grafted specimens from normal ones‡).

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*That the union of such differently oriented parts is easy to accomplish is manifest from all the recent experiments in the transplantation of animal tissues as is seen from the results of Born, Wetzel, Joest, Morgan and myself.

†This is admirably illustrated by Mall's (16) experiment in reversing a coil of intestine in the dog. The reversed coil heals perfectly with the non-reversed part, but the peristaltic movement takes place in it as if it had never been tampered with. The heaping up of the intestinal contents at the suture eventually results in the death of the animal.

‡This is in substantial agreement with Wetzel (26) who concludes from his experiments upon Hydra: "Dies deutet darauf hin, dass vielleicht weniger polare Gegensätze als überhaupt Abweichungen von der normalen Gestalt die beschriebenen Vorgänge bedingen." In his second paper, Wetzel (27) distinguishes between "Regenerationspolarität" and "Verwachsungspolarität." While these expressions do not seem to me to be quite apt, the distinction made above by me agrees essentially with Wetzel's.

§Vöchting (92) on the other hand, from his elaborate study of plant-grafting comes to the conclusion that the polarity of the vegetable cell is comparable to the polarity of the magnet. In the theoretical discussion of his results he states (page 156): "Wohl wären wir im Stande, den Gegensatz der Pole dadurch festzustellen, dass wir die gleichnamigen und ungleichnamigen in Berührung brächten und dadurch zu der Regel gelangten, dass die ersteren sich abstoszen, die letzteren sich anziehen,—ein Anziehen und Abstoszen, das sich hier freilich nicht in freien Bewegungen, wohl aber im Wachsthum äuszert. Wir verführen sonach ganz wie der Physiker, der die Eigenschaften der verschiedenen Pole des Magneten auch dadurch bestimmt, dass er sie auf einander wirken lässt."

*Born made extensive experiments in combining larvae of different species or even genera, as in the case of Rana esculenta and Bombinator igneus. Owing, however, to unfortunate circumstances, none of these combined specimens survived the operation much over three weeks.

†This is different from the result which Wetzel obtained from grafting together hydras of different species (grisea and fusca). In this case, even though there be a union between the two parts, each part completes itself by regeneration of what is missing. But when the two pieces (similarly oriented of course) are of the same species, no regeneration occurs, for then the two unite into one complete individual. Wetzel calls attention (page 88) to the difference between his results and Born's, who found no regeneration from either when two pieces of different species were joined. His objection to the comparison between the results in Hydra and the Amphibian embryo, viz., that in the latter scarcely any regenerative capacity is present (referring of course to the trunk-region), would not hold in the case of my experiments with the tail, where the power of regeneration is very great. But then, as Wetzel points out, the union between pieces of hydras of different species is never complete and the one part does not react to stimuli applied to the other. Therein seems to lie the chief ground for the difference between his results and Joest's (Lumbricidae), with which latter mine agree in essentials.

‡The specific markings in later stages are due to the presence of large chromatophores, situated for the most part in the tissues underlying the epidermis. It seems certain that such cells often cross the boundary for a short distance from one species to the other, although it is difficult to demonstrate this actually, since the

The regenerative power of the transplanted tail is also normal as is seen from the following experiment:

Case 13.—The tail of a larva of R. virescens was replaced by the tail of a larva of R. palustris, in the manner described above (page 175). Forty-eight hours later, at which time the sketch (Fig. 21) was made, the tail was amputated. The epidermis from the virescens body had then pushed out considerably over the root of the tail, so that in cutting almost all of the grafted epidermis (stippled in the figure) was removed. But a considerable portion of the underlying organs of the transplanted piece (shaded in the figure) remained, and it was from this component that regeneration took place in all the tissues with the exception of part of the epidermis. The newly grown tail was of normal form; and, as far as could be observed, it had the characteristics of the species of the grafted stump (palustris) and not those of the body (virescens) (Fig. 4, Pl. X).

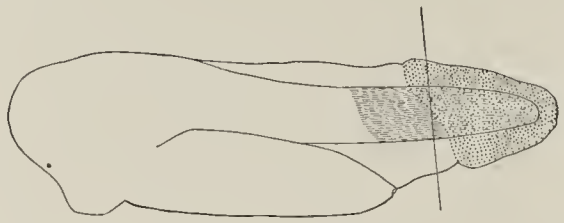


Fig. 21.—Rana virescens with tail of Rana palustris, two days after transplantation, showing place where tail was amputated. ×11. For regeneration see Fig. 4, Pl. X.

This was seen in the character of the pigmentation and especially in the absence of the large black blotches along the side of the tail, which are found constantly in the regenerated appendages of R. virescens. In spite of the insignificant size of the grafted stump as compared with the whole body, and in spite of the fact that the nourishment conveyed to the growing appendage is brought there in blood which is largely derived from the body, the tissues maintain their specific characters.* (See foot-note page 191.)

A number of specimens in which each of the two components formed approximately equal parts of the individual were kept under observation. In all the cases in which this combination resulted successfully, R. virescens had been used as the head component and R. palustris as the caudal. Although the reciprocal combination was tried in a considerable number of instances, for some unknown reason it never resulted in success. The palustris embryo being somewhat larger than the other, it was found advisable to cut off the head of the former in the constricted region just behind the gill arches, while the latter was cut somewhat further back where its circumference is greater. On this account at least part of the pronephros and possibly also the rudiment of the fore leg were duplicated, but without disturbing effect.

Many of these larvae (nearly thirty) gave promise of doing well. They passed through the critical stage when the supply of food-yolk is exhausted, and began to eat and to shift for themselves. All of them showed the characteristics of R. virescens in the head and those of R. palustris in the body and tail. However, no sharp line dividing the two constituents could be observed after the yolk and ectodermal pigment was gone (Fig. 5, Pl. X).

One by one they became weakly, decreasing considerably in size and finally dying unless preserved. Several of these larvae lived over three months; the others succumbed at various intervals.

Only one (Fig. 5, Pl. X) passed through its metamorphosis. The operation in this case was performed on April 6. In its larval history there is nothing of individual importance to note. On August 7, its forelegs broke through. Its metamorphosis was completed on August 10. The resulting frog, perfectly normal in form, was much smaller than usual, being but 1.7 cm. long.* It was kept in a terrarium in which it had access to a pool of water. Its instincts were apparently normal, and it would spring about catching small flies and other insects, which were supplied in abundance. On August 27 it died suddenly, death being probably due to overfeeding. The specimen was placed in formalin a few minutes after death ensued, and was afterwards photographed (Fig. 25, Pl. XI), magnified approximately two and a half diameters.

The little frog is darker than any of the specimens of either R. virescens (Figs. 23 and 24, Pl. XI) or R. palustris (Fig. 26, Pl. XI) which I have examined.† The trunk has distinctly the markings of R. palustris with the dark-brown squarish spots on the back arranged in two rows on a lighter field, which, in the present case, is much darker than usual.‡ The spots are relatively larger than in the normal palustris, although I have had no specimen which was as young as this for comparison. Both pairs of legs correspond to the palustris type in the arrangement of the tubercles as well as in the markings of the skin.§

The head does not seem at first to resemble that of the normal virescens very strikingly. The snout is much too blunt and the distance between the eyes too great. These are, however, characteristics of the young individual. The unusual protrusion of the eyeballs is a post-mortem change. There is one round spot in front of the palustris region, and this is a virescens marking, and the characteristic spot on the top of

markings are referable to characteristic groupings of the pigment cells rather than to differences between the individual elements of the two species. These circumstances are unfortunate for the present purpose and conspire to add a source of error in the interpretation of observations.

*I had hoped to obtain more definite evidence concerning the influences which regulate regeneration, from experiments carried out upon these lines. But owing to unfortunate circumstances most of the larvae of this series died. Besides, all regenerated tails deviate somewhat from the normal type, especially as regards pigmentation, which fact would bring in a considerable element of uncertainty, and in the tail I have not been able to find any other characters which could with safety be considered diagnostic of either species.

*The larvae of R. virescens do not usually complete their metamorphosis until the following season.

†For descriptions of these species, see Cope (5).

‡The dark color has been considerably exaggerated in the figure, so that the markings on the body hardly show.

§In grafting, the rudiment of the anterior extremity was left intact in the posterior (palustris) part, and at least part of the rudiment was left in the anterior (virescens) component.

the orbit is present, though not very well defined. The lines running from the nostrils to the eye and to the shoulder are not very distinct. But what is more important than these color-markings, the arrangement of the vomerine teeth is like that in R. virescens. It was observed too that, especially in the virescens part, the characteristic markings made their appearance little by little. Had the frog lived longer, it does not, therefore, seem improbable that this part would have become more virescens-like. At any rate, the deviation of the head from the normal virescens type is not in the direction of the palustris type. And a similar statement may be made with regard to the body, for its general darkness in color can scarcely be regarded as a virescens character. Each component, then, maintains, on the whole, its own specific characters, subject, however, to certain non-specific modifications, as in the cases where the tail alone is transplanted. Of course the blood derived from the two parts is completely mixed and there is beyond doubt an interlacement of nerve-fibers both in the spinal cord and peripherally. A portion of the palustris component is covered over by virescens epidermis (page 177) and the virescens nerves running to this region must pass through the connective tissue of the palustris constituent. Wandering cells, pigmented and otherwise, no doubt cross the border from one component to the other. But all of these occurrences are found in the development of the normal individual, and are of the nature of the mixing of tissue-elements, rather than a blending of their characters. In addition to this, the tissues of the two species undoubtedly may influence one another in various ways, as is well known in the case of plants. A discussion of these influences in the absence of more material would be premature. It will suffice here to repeat that the two components do not modify one another in the direction of their respective species.*

Notwithstanding the fact that the grafted appendages described in the beginning of this section are nourished and grow normally at first, their later history, as seen from the description of the following individual cases, seems to indicate that the harmony between the tissues of the two components is not permanent.

Case 14.—A tail of R. virescens was grafted in normal position to the body of a palustris larva. The operation was performed on April 27th, the union of the parts being very exact. On May 20th, twenty-three days later, signs of degeneration were observed in the tip of the transplanted piece.* The degeneration was at first confined to the tip, and was apparent as a slight shrinking of the tissues of the fin-fold at that place, so that the distal end of the notochord projected freely beyond, as may be seen in Fig. 7, Pl. X, which is taken from Case 16. After this, atrophy proceeded very rapidly, although not so rapidly as during normal metamorphosis. On May 31st, eleven days after first being noticed, almost the whole of the transplanted tissue had become involved in the degeneration (Fig. 8, Pl. X). At the time degeneration began, and even after it had proceeded so far, the hind extremities were represented by the merest knob-like projection on each side of the base of the tail. No metamorphosis followed the resorption of the tail. Degeneration was confined exclusively to the grafted tissue, and involved eventually the whole of it, although it was never entirely absorbed. The larva was apparently well nourished and grew rapidly, though its appearance was rather grotesque owing to the curious shape of the remains of the tail (Fig. 9, Pl. X). On July 28th the specimen was preserved.

Case 15.—This has a history almost exactly similar to the foregoing. The atrophy of the tail was somewhat more complete (Fig. 10, Pl. X).

Case 16.—The combination was the same as in the foregoing. The operation was performed on April 21. As in the previous cases degeneration began early, but did not proceed beyond the initial stages (Fig. 7, Pl. X) until several months had elapsed, but instead the tail grew to an unusually great length. The grafted part in which the blood supply was excessively rich, was distinctly marked off from the root by the smaller size of the axial musculature (Fig. 11, Pl. X). On July 26 a sudden change was observed in the tip of the tail, which then became very deeply pigmented. Examination with the microscope showed that the blood-vessels throughout the tail were distended, and that the circulation in them had practically stopped. At this time the hind legs were fairly well developed, although by no means advanced as is usual at the time of metamorphosis. Degeneration with absorption of the tissues proceeded rapidly, but the specimen was preserved two days later before the process was completed.

Case 17.—In this case the reciprocal experiment was performed. A palustris tail was trasplanted to a virescens body. The grafting was done April 13. Not until May 31 were any signs of degeneration noted (Fig. 12, Pl. X). Atrophy of the tail proceeded with but little apparent resorption of the tissues, so that six weeks later the appearance of the larva in gross was quite different from either of the others just described (Fig. 13, Pl. X). The axis of the tail was considerably shriv-

* This is in agreement with the conclusions reached by Vöchting (24) from a study of plant-grafting. After summing up the various influences of stock upon scion he concludes (page 112): "Zu den genannten drei Gruppen von Einflüssen würden sich, wenn ihre Existenz erwiesen wäre, als vierte die gesellen, welche als specifische unterschieden werden mögen. Das Eigenthümliche ihrer Wirkung würde darin bestehen, dass sie Veränderungen in der specifischen oder systematisch gegebenen Form hervorriefen, somit also von sehr tiefgreifender Art wären.—Derartige Einflüsse, angeblich zwar oft beobachtet, haben sich bei näherer Untersuchung in der Regel als Täuschungen erwiesen. Uns selbst ist es in keinem unserer zahlreichen Versuche gelungen, ihre Wirkung wahrzunehmen.—Durch solche Einflüsse wurden auch die sogenannten Pfropfhybriden hervorgerufen, deren Existenz aber, wie früher ausgeführt, durchaus zweifelhaft ist."

Also Joest (12), who made numerous successful experiments in uniting earthworms of different species and genera, obtained like results. In all heteroplastic combinations each part was found to preserve its specific characters, coloration included, even down to the minutest observable details. And even in cases where one of the components regenerates a lost part, no influence upon the regenerated part could be traced to the component of the other species.

* In the history of a composite specimen where the tail half of a larva of Rana arvalis had been transplanted to the belly of a larva of Rana esculenta, Born mentions that the tail tip of the former showed signs of atrophy after a short time, page 561.

eled but not much shortened. No further changes were noticed between July 15, when the photograph was taken, and August 16 when the specimen, otherwise still perfectly healthy, was preserved.

In addition to the four cases just described, there were others in which the incipient stages of atrophy were noted. Two of these were palustris larvae with virescens tails, and two were virescens larvae with palustris tails.*

On the other hand there were three virescens larvae with palustris tails which showed no signs of degeneration in the transplanted tissues. One of these, the case described above, in which a portion of the grafted tail was amputated and allowed to regenerate, was preserved ninety-three days after the operation, and the others, when last observed four months after, were perfectly normal.

Likewise, in some of the cases also described in the second section (page 177), where a small portion of the body, including some yolk, was transplanted along with the tail, similar degenerative phenomena were observed. In all, five specimens were kept for forty days or longer. Two of these, both virescens larvae with palustris tails, became weak, seemed poorly nourished, and died at the expiration of forty and sixty days respectively, without showing any particular signs of atrophy of the tail. In two others, which were otherwise apparently healthy, the tail did degenerate. The one to show it the earlier was a palustris larva with a virescens tail, in which degeneration began about the ninety-fourth day after the operation, and proceeded rapidly in much the same way as in Case 1. The other tail, which began to atrophy on the one hundred and third day, was R. palustris and had been united to a virescens body. This was never absorbed as in the first case, but had an appearance much like that described in Case 16. The fifth specimen was preserved after four months, and at that time was in a perfectly healthy condition.

These cases may be summed up as follows:

Virescens tails grafted to palustris larvae always degenerate (five cases), while palustris tails grafted to virescens bodies degenerate in fifty per cent. (three) of the cases.

When a small portion of the body, including yolk, is transplanted with the tail, degeneration begins later than when the tail alone is removed.

Two possible causes of the premature atrophy suggest themselves. One is that it is due to the operation of grafting itself, perfect as the union of the constituents may appear.† The other and more probable one is that there is an incompatibility between the tissues of the two species whereby the preponderant one poisons, or at least fails to nourish properly, the other, in spite of the perfect anatomical relations.* In favor of this view there is some evidence, even if it is not crucial. In the first place the quantity of the tissue in the smaller constituent is an element to be considered. When part of the body along with a small portion of yolk is transplanted with the tail, degeneration does not begin until very much longer after the operation than in those cases where the tail alone is removed. This occurs in spite of the fact that the former operation involves more vital parts. In the second place, when the palustris tissue preponderates greatly over that of virescens, degeneration takes place in all cases, while in the reverse combination this degeneration does not always ensue, and when it does, it assumes a different form.†

The further discussion of this interesting question must be postponed until a more systematic series of experiments is made, and above all until sufficient material is at hand for a careful histological study of the degenerative processes.

Summary.

1. The embryos of Rana virescens and Rana palustris are markedly different in color. The specific coloration which is due to pigment and yolk granules, is common to all cells. In heteroplastic combinations of embryos of these species, made according to Born's method, it is, therefore, possible to follow in the living specimen, as development proceeds, the movement of any group or layer of cells with respect to the original dividing line between the two constituents.

2. The combination of body and head of one species with embryonic tail-bud of the other, gives the following information concerning the mode of growth of the tail: a) The epidermis passes steadily from the body to the tail, shifting over the underlying structures, so that one week after grafting the original epidermis of the tail-bud covers but about one-third (the tip) of the tail. b) The musculature, spinal-cord and notochord increase in length largely by apical growth, and also, but to a much less extent, by the pushing of segments (about three) out from the trunk to the base of the tail.

3. In the trunk region, the shifting of the epidermis over the underlying organs becomes less in amount as the head is approached.

4. The movement of the epidermis is due to the tension brought about by the rapid apical growth of the tail, and the absence of a corresponding proliferating centre in the epidermis at the tip.

5. The oblique course taken by the cutaneous nerves of the trunk and tail of the full grown larva and frog, in passing from the vertebral column to their ending in the skin, is due to the ontogenetic shifting of the latter from its original position.

* In three of these, degeneration was first noted after the specimens had been stained and mounted. They had lived twenty-five, twenty-one and twenty-seven days respectively. In the fourth, signs of atrophy were observed on the twenty-fourth day. A few days later this specimen died from an unknown cause.

† Unfortunately, the atrophy of the tail was not observed until after the material at my disposal for experimentation was exhausted. It was, therefore, impossible to make the simple experiment of transplanting a tail from one individual to another of the same species. This would either have proved or eliminated definitely this first possibility.

* Disharmonic combinations are well known in plants. See Vöchting (24), page 100. Born (3) also touches upon this question at the conclusion of his paper.

† Of interest in this connection are the results obtained by L. Loeb (15) from the study of transplantation of skin in guinea-pigs. White skin transplanted to a black field behaves differently from black skin removed to a white field. The former sloughs off while the latter persists. Loeb traces this to the superior regenerative power of the dark skin.

6. After amputation of the tail, the peripheral nervous system is regenerated from the spinal cord. First, a single nerve pair arises from cells lying within the cord. Part of these cells pass out upon the nerve-root and form a large ganglion. Later, a few of the nerve-cells wander further peripherally along the nerve-trunk, forming several (at most three) ganglionic cell-groups. These represent the more distally situated ganglia, lost in amputation, which are never entirely replaced.

7. The oral end of an amputated tail-bud has a considerable regenerative capacity, when the bud is transplanted by its distal end to the body of another individual. The structure then regenerated is tail-like in form, no matter to what part of the body it is attached.

8. When transplanted so as to replace a normal tail the resemblance to the latter may become striking. The perfection of the part as a swimming appendage is in such cases dependent upon the exactness with which the corresponding tissues of the respective components are united. If the union is imperfect, forked tails result.

9. The cases in question are not necessarily to be regarded as heteromorphosis (tail in place of head and trunk), for the tail-like appendage is to be considered as an imperfectly regenerated trunk.

10. The position of the reversed tail-stump with respect to the rest of the organism is of importance during regeneration, only in so far as it influences the degree of efficiency of the structure regenerated. Neither the present nor other experiments indicate that the influence of the organism as a whole upon the regenerating part is able to bring forth a heteromorphic structure, functionally adapted out of material which would normally produce something else.

11. In combinations between embryos of two species, each component maintains its specific individuality. The modifications which may arise in either of the components are not of the nature of a blending of specific characters.

12. In combinations where the tail alone is replaced by a tail of the other species, the latter forms at first a perfect substitute for the original tail. Nevertheless, in the majority of cases, the grafted appendage atrophies later and disappears almost entirely, long before the larva undergoes its metamorphosis.

13. When a small portion of the trunk is transplanted along with the tail, atrophy of the latter is considerably delayed.

14. Also when the two components are united in the region of the pronephros, the composite larva grows normally and may remain healthy and vigorous for many weeks. Only in one case, however, did such a specimen complete its metamorphosis. The frog had perfectly normal instincts and power of co-ordination. The portions derived from each of the two species could nevertheless be distinguished clearly by means of color-markings and other specific characters.

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EXPLANATION OF PLATES.

Plate X.

(All photographs taken from the living tadpoles.)

Fig. 1. Rana virescens, normal with the exception of the tip of the tail, which is regenerated. × 2.

Fig. 2. Rana virescens, with regenerated tail. × 3⅓. Note deepness of pigmentation of the tail, especially the large blotches.

Fig. 3. Rana palustris, normal. × 2.

Fig. 4. Case 13. Rana virescens, with tail of Rana palustris, which is for the greater part newly regenerated. × 3.

Fig. 5. Head of larva (including gills) Rana virescens, remainder Rana palustris. Photograph taken one hundred days after operation. × 2. Same individual as frog (Fig. 25).

Fig. 6. Rana palustris, with tail of Rana virescens. Twenty-seven days after operation. Scarcely perceptible signs of atrophy in tail-tip. × 3⅓.

Fig. 7. Case 16. Same combination as Fig. 6. Forty days after operation. Tip of fin-fold atrophied. × 3⅓.

Fig. 8. Case 14. Same combination as Fig. 6. Thirty-five days after operation. Degeneration of transplanted tail, much further advanced than in Fig. 7. × 3⅓.

Fig. 9. Case 14. Seventy-seven days after operation. × 2½.

Fig. 10. Case 15. Same combination as the foregoing. Eighty-one days after operation. × 2.

Fig. 11. Case 16. Eighty-three days after operation. × 2⅓.

Fig. 12. Case 17. Rana virescens with tail of Rana palustris. Forty-eight days after operation (cf. Fig. 7). × 3⅓.

Fig. 13. Case 17. Ninety-three days after operation. × 3.

Fig. 14. Case 1. Rana virescens with regenerated reversed tail of another individual. Regenerated thirty-eight days. × 3⅓.

Fig. 15. Case 1. Regenerated eighty-nine days. × 3.

Fig. 16. Case 4. Same combination as Fig. 14. Tail regenerated forty-two days. Forked spinal cord. × 3⅓.

Fig. 17. Case 2. Same combination as in Fig. 14. Regenerated thirty-seven days. × 3⅓.

Fig. 18. Case 5. Combination as in Fig. 14 except that both larvae are Rana palustris. Tail regenerated sixteen days. × 3⅓.

Fig. 19. Case 10. Rana palustris with reversed tail of another larva grafted to its back. The transplanted tail has regenerated from both ends (twenty-two days). × 3⅓.

Fig. 20. Same combination as in Fig. 19 except that a small portion of yolk was transplanted with the tail. Regenerated sixteen days. × 3⅓.

Fig. 21. Case 12. Rana palustris with accessory tail grafted to the back. Twenty-one days after operation. × 3⅓.

Fig. 22. Case 11. Same combination as in Fig. 21. Sixty-nine days after operation. Accessory tail to a great extent atrophied. × 2½.

Plate XI.

(All specimens preserved in formalin.)

Fig. 23. Rana virescens, adult female just after spawning. × ⅘.

Fig. 24. Rana virescens, adult male. × ⅘.

Fig. 25. Same individual as in Fig. 5. Head, Rana virescens; trunk and limbs, Rana palustris. Preserved one hundred and forty-three days after operation, or seventeen days after metamorphosis. × 2⅓.

Fig. 26. Rana palustris, young specimen. × ⅘.

ENDOCARDITIS DUE TO A MINUTE ORGANISM, PROBABLY THE BACILLUS INFLUENZA.

(PRELIMINARY REPORT.)

By Mabel F. Austin.

(*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*)

Endocarditis of infectious origin is associated with the presence of many species of pathogenic bacteria; although most commonly the result of the invasion of the pyogenic cocci, other bacteria are capable of producing the characteristic lesions of the disease. Since the discovery of the bacillus influenza by Pfeiffer a number of instances of endocarditis accompanying influenza have been described clinically, but thus far, although this micro-organism has been found in various locations in the body, such as the lungs and the meninges, where it has set up inflammatory processes, it has not been demonstrated in the anatomical lesions of endocarditis. There have come to autopsy in the pathological laboratory during the last three years three cases of endocarditis in which bacilli were found in the lesions of the heart-valves agreeing morphologically with the influenza bacillus, and probably identical with this organism. As the cases are of interest on account of their probable etiology they will be reported briefly in this place.

Case 1.—C. K. Colored. Male, age 20. Autopsy by Dr. Flexner, 3/21/96.

Anatomical Diagnosis.—Acute ulcerative and chronic proliferative endocarditis affecting the mitral, aortic and tricuspid valves; mitral stenosis and insufficiency; rupture of chordae tendineae of mitral valve; perforation of aortic segments;



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adhesion of leaflet of tricuspid valve to ventricular wall; globular heart thrombus; cardiac hypertrophy and dilatation; compression, congestion and infarction of the lungs; hemorrhagic nephritis; oedema.

Only that part of the protocol relating to the heart will be given. The organ is enlarged, weighing together with the pericardium 1050 grams. The hypertrophy affects both sides. The tricnspid valve is the seat of thickening and the segments have become nnited. The chordae tendineae are likewise thickened and contracted and the trabecnlae and papillary muscles are hypertrophied. The cardiac muscle is the seat of marked fatty degeneration. In the apex of the right ventricle there is a globnlar thrombus lightly attached to the wall. The left ventricle is especially enlarged, all the parts being hypertrophied. The chordae tendineae are diffusely thickened, and they are also the seat of minute excrescences between which small erosions exist. Similar vegetations cover the margins of the segment of the mitral valve and the endocardium of the auricle. A tendinous cord proceeding from the right papillary muscle to the mitral valve is ruptured and the fresh edges of the torn thread are covered with recent thrombi. The leaflets of the valve are grown together and thickened. A considerable mass of vegetations extends upwards from the aortic segment of the mitral valve to the aortic valve, covering the inner surface of the aortic segments. Several perforations exist in the right segment.

Bacteriological Examination.—The cover-slip preparations made from the vegetations of the cardiac valves are crowded with micro-organisms. These consist of small bacilli, usually straight, but sometimes curved. They stain both solidly and at the poles. These rods are chiefly free, but many are also contained within the protoplasm of leucocytes. No other form of micro-organism was found in the cover-slips. Cultures made upon agar from the unopened heart gave no growth. After opening the heart second cultures were made, and these grew a variety of micro-organisms which were regarded as accidental. The minute bacillus described was not present in the rank growth.

Case 2.—W. W. Colored. Male, age 37. Autopsy by Dr. Flexner, 10/22/96.

Anatomical Diagnosis.—Chronic mitral endocarditis and stenosis; sclerosis of coronary arteries; vegetative and ulcerative endocarditis of mitral and aortic valves; chronic passive congestion.

The heart is hypertrophied, its weight being 470 grams. The leaflets of the mitral orifice are thickened and grown together, and the orifice is narrowed. The chordae tendineae are also thickened and shortened. The edges of the valve are incompletely covered with vegetations which can be traced from this situation to the aortic valve, the middle segment of which shows two perforations. The tricuspid valve is free.

Bacteriological Examination.—Films from the mitral valve show great numbers of short slender bacilli, sometimes slightly curved. These show distinct polar staining. By Gram's stain they are completely decolorized. Cultures upon agar-agar were negative. Sections of the mitral valve stained for bacteria showed large numbers of organisms similar to those described in the cover-glass preparations.

Case 3.—G. M. White. Age 17 years. Autopsy by Dr. Flexner, 2/22/98.

Anatomical Diagnosis.—Stenosis of the pulmonary artery; chronic and acute endocarditis of pulmonary valves; vegetative pulmonary arteritis; heart hypertrophy; hemorrhagic infarction of lungs; chronic passive congestion.

The heart is enlarged, weighing 400 grams. The mitral and aortic valves are normal. The tricuspid valve, except for a hard calcified nodule is also normal. The pulmonary orifice is stenosed; the leaflets of the valve are grown together, the segments being diffusely thickened. The free edges of the valves are covered with vegetations which extend into the pulmonary artery and its primary branches.

Bacteriological Examination.—Film preparations made from the vegetations upon the pulmonary valve and artery show many polymorphonuclear leucocytes with fragmented nuclei. The protoplasm of these cells is filled with minute bacilli, and similar organisms are found outside, probably liberated by disintegration of the cells. They are straight or curved and stain either uniformly, or more deeply at the poles. Cultures on agar-agar from the unopened heart were negative. After opening the heart and some handling a second series of cultures was made, which however became contaminated. The minute organism seen in the films did not appear in these contaminated cultures. Sections of the pulmonary valve and artery show chronic fibroid thickening with recent thrombi. In these thrombi large numbers of minute bacilli were found. Sections of the lung show, besides the chronic congestion, similar bacilli which occupy the alveolar spaces.

The above cases present an infection of the endocardium with minute bacilli possessing characteristics in common. The morphology of the bacilli, their staining reactions, and their difficulty of culture agree with the properties of the bacillus influenza. Unfortunately, the organisms were not obtained in cultures, so that one link in the chain of proof that the organism is the bacillus of influenza cannot be supplied. Perhaps the conditions under which the cultures were attempted may be responsible for the failure to obtain growths even when suitable media were employed. On the other hand the vast numbers of organisms described which were found upon the diseased heart-valves leave no question of their causal connection with the pathological process.

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OBITUARY.—EDWARD P. McKEOUGH.

At a meeting of the Class of Nineteen Hundred and One, of the Johns Hopkins Medical School, held October the twenty-first, Eighteen Hundred and Ninety-Nine, the following resolutions were adopted:

WHEREAS, It has pleased God, in his infinite wisdom, to remove from our midst our beloved friend and classmate Edward Patrick McKeough; therefore be it

Resolved, That we, the members of the Class of Nineteen Hundred and One, of the Johns Hopkins Medical School, do deeply regret the loss of one who has been a true and loyal man, and whose life and character will ever be an example for his friends to follow; and

Resolved, That we express to his family our most heartfelt sympathy in their great bereavement; and

Be it further Resolved, That a copy of these resolutions be sent to his family and published in the BULLETIN of the Johns Hopkins Hospital.

H. P. PARKER,
R. T. COMER,
MARION WALKER,
J. R. BOSLEY,
} *Committee.*

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Report of Gynaecological Cases. Dr. KELLY.

CASE 1. *Extensive Destruction of the Sphincter.*—This patient was an old syphilitic with extensive ulceration of the bowel which had been present for a number of years and for which a number of operations had been performed. The diseased area could be distinctly felt through the vagina as a rigid fibrous cord extending well up back of the cervix and in some of the operations (she had had 19) the sphincter had been destroyed anteriorly, leaving a boat-shaped scar.

I operated on the 23rd of March of this year and she remained in the hospital until the 25th of April. I performed the following operation, desiring to get rid of this restricted area, and restore the function of the bowel so that she could have easy passages and be able to control them: I divided the septum freely with a pair of scissors, cut across the sphincter and turned it over as a flap, making a U-shaped incision with its convexity forward. Then I followed up the bowel, catching it with forceps and pulling it down and dissecting it out on all sides with scissors. I tied a great many small vessels, dissected out the levator ani, opened the peritoneum and found that at a point opposite the middle of the cervix the lumen of the bowel became normal. I cut the bowel at this point, brought it down and attached the posterior end just behind the sphincter. Then, by a somewhat complicated plan of suturing, I attached the bowel anteriorly and at the sides to restore the sphincter. The result was all I could have desired. She made a perfect recovery and now has entire control over the function of the bowel.

CASE 2. *Carcinoma Uteri.*—This patient had probably the most advanced carcinoma of the uterus I have operated upon satisfactorily since I have been at work in this hospital. The lower part of the uterus was destroyed and the disease extended anteriorly so far that there was some doubt about the involvment of the floor of the bladder. She stood a prolonged operation of about two hours very well. Had she not been in such good condition at the time I could not have attempted it. I first introduced bougies into each ureter so as to have them under observation at all times. This is a *sine qua non* to success in all such operations, for we can at any moment see just exactly where the ureters are. I then made an incision in the vault of the vagina and began by freeing the bladder from the vagina and separating it from the uterus; then catching the uterus at the fundus I pulled it down through the opening in the vaginal wall. Next I tied off the vessels of the broad ligament in the upper part, split the uterus in two, which made it more movable, thus enabling me to turn the two portions down into the vagina and so get at them more readily. I removed first the easiest side, taking care to get as far as possible from the uterus and avoid the ureter which was constantly in view; I then attacked the more difficult side. When I got down to the base of the broad ligament, I was able to show very well the risks one experiences when the ureter is not catheterized. It could have been doubled on itself and if the bougie had not been in place I might have felt perfectly safe in thinking it at some other point than the place it really occupied. I amputated the diseased portion of the ureter, incised the bladder and stitched the ureter to it. The patient has done very well ever since and there is every reason to believe that she will make a good recovery.

I think we are going to occupy a very different attitude towards these carcinoma operations in the future. We are coming back to the vaginal operation, but this will be performed in a different way from former methods. Fifteen years ago the uterus was always removed by vaginal hysterectomy. It was skinned out, this being done to avoid the danger of tying the ureters, but, of course, bits of carcinomatous tissue were always left in. Some of us, to avoid this, went over to the abdominal route. Drawing our inferences from the operations performed on the surgical side of the house in breast cancer, we thought we should get better results by removing the glands with the uterus. We did some satisfactory operations, taking out all the pelvic glands we could find. Very painstaking and thorough examinations made by Dr. Cullen in our laboratory showed, however, that our conclusions were not warranted and that the disease

extended directly up from the cervix, the glands being involved only in the late stages, or in cases that were not operable. I have, therefore, come back to the vaginal operation, performing it, however, in a new way. I make an incision, begin above and work down, splitting the uterus and with bougies in the ureters so as to know at all times where they are. All that is necessary is a patient that has not been so weakened by hemorrhages or disease that she will not be able to stand a prolonged operation. I am glad for many reasons to come back to this operation again.

Case 3. *Excessive Growth of Fat.*—A patient thirty years of age came in the other day because of an enormous development of fat in the body and I removed the large mass before you from the abdominal wall. She had a pendulous abdomen and was glad to get rid of some of the superfluous fat so as to enable her to walk around with comfort. Her weight was 285 pounds and this mass, which is larger than the ordinary woman's whole belly, was removed, the edges of the wound being brought together without tension. It weighs 7,450 grams and forms an interesting contrast to a small lipoma of the thigh about the size of my fist that I removed a few days before.

Dr. Welch: It is of interest that the prognosis is relatively favorable after hysterectomy for uterine cancer. This is, of course, due to the late period at which metastases are prone to appear. There are two forms of cancer of the uterus, the flat-celled of the cervix and the adeno-carcinoma of the body. The latter originates in the mucous membrane, extends down slowly into the wall of the uterus and it is a significant fact that the metastases occur generally quite late. It is as if the wall of the uterus was a sort of case and prevented the ready entrance of the cells into the lymphatic or blood current, as occurs with cancers developing in the interior of ovarian cells. The flat-celled epithelioma does not form secondary deposits in the lymphatic glands so readily as most cancers do and this is true in general of flat-celled epithelioma.

NOTE ON NEW BOOKS.

The Mechanics of Surgery: comprising detailed descriptions, illustrations and lists of the instruments, appliances and furniture necessary in modern surgical art. By Charles Truax. (*Chicago*, 1899.)

The object of this book is to present to surgeons careful detailed descriptions of instruments used in surgical operations, and also of instruments for general medical research, such as microscopes, thermometers, stethoscopes, sphygmographs, aesthesiometers, dynamometers, etc. The work seems carefully and judiciously done, and the result is a book of great utility to the surgeon and physician. The descriptions of instruments are very complete, and the accompanying illustrations are helpful to those who wish to identify instruments and determine in their own minds what they may use for particular operations. The information is exact and covers the more recent surgical appliances like Laplace's anastomosis forceps and Murphy's button. It is difficult to call to mind any surgical instrument of permanent value which may not be found described or pictured in this handsome volume of 1000 pages. The author deserves great credit for the thorough manner in which he has worked out his ideal of the utility of such a book. He has avoided trenching upon technical ground, and yet has produced a very helpful handbook.

BOOKS RECEIVED.

Seventeenth Annual Report of the Provincial Board of Health of Ontario. Being for the year 1898. Printed by order of the Legislative Assembly. 1899. 8vo. XXXVIII + 322 pages. Warwick Bros. & Rutter, Toronto.

Report of the Commissioners of the District of Columbia for the year ended June 30, 1898. Vol. III. [Health Department.] 8vo. 261 pages. 5 maps. 1898. Government Printing Office, Washington.

United States Treasury Department, Marine Hospital Service. Centennial Year. Annual report of Supervising Surgeon General of the Marine-Hospital Service of the United States for the fiscal year 1898. 8vo. 855 pages. 1899. Government Printing Office, Washington.

A History of the Chronic Degenerative Diseases of the Central Nervous System. By Thomas Kirkpatrick Monro, M. A., M. D., 1895. 8vo. 82 pages. Alex. MacDougall, Glasgow.

Atlas of Diseases of the Skin, including an Epitome of Pathology and Treatment. By Prof. Dr. Franz Mračeк, of Vienna. Authorized translation from the German. Edited by Henry W. Stelwagon, M. D., Ph. D. With 63 colored plates and 39 full-page, half-tone illustrations. 1899. 12mo. 199 pages. (Saunders' Medical Hand-Atlases). W. B. Saunders, Philadelphia.

The Mechanics of Surgery: comprising detailed descriptions, illustrations and list of the instruments, appliances and furniture necessary in modern surgical art. By Charles Truax. 1899. 8vo. 1024 pages. Chicago.

Report of the Board of Managers of the Pennsylvania Hospital to the Contributors, at their annual meeting held fifth month second, 1898. Comprising the report of the department for the sick and wounded and of the departments for the insane, etc. 8vo. 108 pages. 1897–98. Avil Printing Co., Philadelphia.

Thirty-fifth Annual Report of the Trustees of the Boston City Hospital, with report of the Superintendent, February 1, 1898, *to January* 31, 1899, *inclusive.* 1899. 8vo. 206 pages. Municipal Printing Office, Boston.

Illustrirte Rundschau der Medicinisch-Chirurgischen Technik. Herausgegeben von Gustav Beck. 1898. Jahraang 1. 8vo. 416 pages. 1898. K. J. Wyss, Bern.

Mount Sinai Hospital Reports. Volume one for 1898. Edited for the Medical Board by Paul F. Mundé, M. D., LL. D. 8vo. 343 pages. 1899.

Thoracic Resection for Tumors Growing from the Bony Wall of the Chest. By F. W. Parham, M. D. 1899. 8vo. 147 pages. New Orleans.

Cavendish Lecture: On the Etiology and Diagnosis of Cerebro-Spinal Fever. By William Osler, M. D. [Reprinted from the "West London Medical Journal."] 1899. 8vo. 46 pages. John Bale, Sons & Danielsson, Ltd., London.

An Introduction to Dermatology. By Norman Walker, M. D. With a frontispiece. 29 plates and 34 illustrations in the text. 1899. 8vo. 247 pages. John Wright & Co., Bristol.

Our Baby: For Mothers and Nurses. By Mrs. Langton Hewer. Sixth edition. Revised, 1899. 12mo. 154 pages. John Wright & Co., Bristol.

Metropolitan Asylums' Board. Annual Report, 1898, Vol. I. 1899. 8vo. 114 pages. McCorquodale & Co., Limited, London.

Metropolitan Asylums' Board. Annual Report, 1898, Vol. II. Thirteenth Report of the Statistical Committee with Appendices. 1899. 8vo. 192 pages. McCorquodale & Co., Limited, London.

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SCIENTIFIC LABORATORIES.*

By Professor William Keith Brooks *of Johns Hopkins University.*

I regret that I am one of those who have learned to call the century that is now drawing to a close *our* century. I find my chief recreation and inspiration in reflecting upon that great extension of natural knowledge which we owe to the master minds of the nineteenth century. I would not have you infer that I do not hope for a share in some of the great things of the future, although I do find it hard to remember that the difficulties which our great men have overcome, their struggles, and failures, and successes, are even now becoming ancient history; that the thoughts and the hopes of the audience which is now best worth addressing are in the future. The great men of the nineteenth century have won results that can never be forgotten; but the sympathy of those who remember the small beginnings of these great results, the patience, the courage, and the untiring industry by which each little step was won, will soon be a thing of the past.

Some of you, who hear me to-day, may hope to see things that our poets have only dreamed—many things that no poet ever has dreamed, no prophet foreseen, things that it hath not entered into the heart of man to conceive; but, as you enter upon your inheritance of great opportunities, will it not be well to remember that they are an inheritance? Not that it will matter to the men who are gone, whether they are remembered or forgotten. It has been my good fortune to know some of the great scientific discoverers of our day, while I believe that I know others still more intimately through their works and the story of their lives, and through the records of their influence upon others; and I believe I may honestly assert, in their name, that hope of remembrance by posterity had little part in their inspiration. It is not in their interest, but in yours, that I ask you to be mindful of your debt to them. If the men of the twentieth century find themselves better equipped for the discovery of truth than any who have gone before, if they have more and better means for the extension of natural knowledge and the relief of man's estate, they owe most of their advantages to the pioneers of the nineteenth century. Now, a pioneer is a man who has faced difficulties; one who has made his own opportunities. Often is he one who has brought out of this struggle those high qualities of fearlessness, and independence, and tenacity of purpose, and single-minded honesty, which, important everywhere, are absolutely essential for progress in science. To be what is commonly called self-made, either in generations or in men, is not a distinction but an advantage. It is for this reason that I ask you to keep warm your sympathy for the men who have done great works in science in the past, with scanty facilities, and in the face of difficulties.

In order to duly estimate the full importance and the grandeur of the century which is now nearing its close, especially as regards man's increased power over nature, and the application of that power to the needs of human life, we must, says Wallace, compare it, not with any preceding century, or

* Address delivered at the dedication of the Biological Laboratory of Western Reserve University, June 13, 1899.

even with the last thousand years, but with the whole period of human history; yet it is not the progress in science which this century has made, but the means and the opportunities for still greater progress which it has put into the hands of future generations, which has seemed, to thoughtful men, to be its great distinction. One of the most important instruments for scientific discovery which the nineteenth century has put into the hands of the twentieth is the scientific laboratory. This too is one of its latest gifts, for it is only within very recent years that all the books and apparatus and appliances and material that are needed for the advancement of great departments of natural knowledge have been brought together in buildings constructed for the purpose, and placed under the supervision and direction of investigators who are qualified to use all these great advantages and opportunities for the promotion of knowledge and for the instruction and training of students. The last quarter of the nineteenth century is emphatically the birthday of laboratories, although the needs of different departments of knowledge were not all recognized or provided for at the same time. The chemical laboratory has come down to us from the days of alchemy, and we are told that there have been astronomical observatories in Europe for five hundred years, but most of the scientific laboratories which are so characteristic of our day are very modern. The form of application to the U. S. Treasury for alcohol for scientific purposes free of duty says that this law "is not held to include 'physical,' 'mechanical,' 'electrical,' or 'pathological' laboratories, or any other laboratory which has been developed since Feb. 21, 1873, when the law was passed."

It was my good fortune to have a share in one of the first attempts to organize laboratory instruction in natural science in Cleveland, and I hope you will pardon me if, on this occasion, my mind runs back to this old undertaking. In 1875 three young men who had begun to train themselves as naturalists came together for their summer vacation at their homes in Cleveland. They were Theodore B. Comstock, afterwards President of the University of Arizona; Albert H. Tuttle, now Professor of Biology in the University of Virginia, and myself. We were filled with enthusiasm for our work, and, like all earnest students from Chaucer's day to this, as glad to teach as to learn, and we determined to organize a summer class for laboratory instruction in zoology and botany. Money for our expenses was liberally supplied by R. K. Winslow, Leonard Case, and other citizens; the authorities granted us the use of the old high-school building on Enclid avenue, near Erie street, and we were soon able to issue notices of our undertaking, and invitations to all who wished to join the class, asking them to do so without the payment of any fee. Some twenty-five were soon enrolled, most of them teachers, some from a distance, and work was begun with a class which shared all the earnestness and enthusiasm of their instructors. We had daily lectures or demonstrations, followed by four or five hours of work in the laboratory, while two afternoons in each week were given to excursions to Rocky River, Cuyahoga Falls, and other places favorable for the out-of-door study of nature. As a small steamboat had been placed at our service, we made two excursions upon the lake, and thus gave to the class an opportunity to learn the use of the naturalist's dredge for collecting the animals of the bottom. Our work was, in part, the study of the animals and plants which we obtained on these expeditions, and we also made use of a supply of marine animals which had been gathered for the purpose at the seashore.

I do not know that I can trace any continuity between this summer class of 1875 and the beautiful and thoroughly equipped Biological Laboratory in which we have met to-day; but the anecdote may serve to remind some of those who will, in future years, make use of the resources and facilities which are here so liberally supplied, that they owe the modern scientific laboratory to men who were, for the most part, obliged to do their work without aid from others. In making this great gift to the men of the twentieth century, they of the nineteenth bid you "Godspeed" in the use of this great agent for the service of your race, for they are sure that, in your hands, it will make known to mankind wonders of nature which eye hath not yet seen nor ear heard. They charge you, however, not to forget that opportunities do not make success; for the greatest success, in science as in all other works, has been won by men who made their opportunities. A good horse helps the traveler on his way, but he who rides because he is not able to walk is not likely to make a long or a successful journey. Some tell us that there is a law of evolution, a necessary principle of universal progress, that carries things along; that the great advances in scientific knowledge which have been made in our day will continue to run on by virtue of this principle—that if the heirs of all the ages will but wait until they come to man's estate their inheritance will drop into their laps. I have no patience with this sort of nonsense. Natural laws are not agents who do things, but generalizations from an experience which seems to teach, among other things, that progress is neither necessary nor universal. I am sorry to say that my own experience of life tells me that it is, unfortunately, a little easier to stand still or to slip backward than to go up hill. The only necessary law of progress that I can discover is that it is necessary to fight pretty hard for everything worth the getting, and that it is no light or easy task to keep what has been won. There have been dark ages in human history, and periods of great intellectual activity have been followed by periods of stagnation and decay. Natural knowledge is not like the corn that grows while we sleep; for, if the price of civil liberty is eternal vigilance, the price of intellectual liberty is vigilance even more alert and untiring.

The scientific men of the nineteenth century do not fear for their successors. They are confident that you will not be found wanting in the high qualities that win success, although the road ahead of us looks very much like that over which we have come, with a few smooth, easy places, and many that are rough and hard. They have no fear that you will be pauperized by prosperity, but if you take it for granted that you are destined to great things because you have great opportunities and great advantages, your end will be disappointment and decay; for you are destined to do nothing except what you determine to do, and fight for, and succeed in doing. To you they intrust the full fruition of the scientific laboratory. They consign it to you with confidence, and without fear; but they do not believe any one will charge them with boasting, if they assert that it has not been entirely fruitless in their hands; for

a history of scientific laboratories during the last thirty years would be a history of all that is most notable and distinctive of this period, as compared with those that have gone before. It is a history that no one man can write, and a bare enumeration of the discoveries that have been made by the methods of the laboratory would far exceed the limits of my time and of your patience.

Wallace, in his recent book on the Wonderful Century, gives a list of the inventions and practical applications of science which are perfectly new departures, and which have also so rapidly developed as to have profoundly affected many of our habits, and even our thoughts and our language; so that they are comparable, in their effects upon mankind, to the telescope and the printing-press and the mariner's compass and geometry and writing. He finds that while there have been only seven of these scientific inventions of the first rank, in all human history up to the end of the eighteenth century, there have been thirteen in the nineteenth, and of these thirteen, eleven are the products of the laboratory. The seven great inventions which Wallace enumerates for all preceding ages, are alphabetical writing, Arabic numerals, printing, the thermometer and barometer, the telescope, the steam-engine and the mariner's compass; while his list for the nineteenth includes railways, steamships, electric telegraphs, the telephone, lucifer matches, gas illumination, electric lighting, photography, the phonograph, Roentgen rays, spectrum analysis, anaesthetics, and antiseptic surgery. Whether we agree with Wallace that these thirteen are the greatest inventions of our century or not, all will agree that they are very great inventions, with boundless possibilities for the service of man, and that most of them are the products of the methods of the laboratory.

But I would not have you suppose that they are the greatest or the best products of work in laboratories; for the improvement in our material resources is not the end which thoughtful men have found most worthy of their devotion. If natural knowledge were only a sort of fairy godmother, ready to furnish her pets with shoes of swiftness, swords of sharpness, and omnipotent Aladdin's lamps, so that they might have telegraphs to Saturn, and see the other side of the moon, and thank God they are better than their benighted ancestors, Huxley tells us that he, for one, should not greatly care to toil in the service of natural knowledge. "I think," says he, "I should just as soon be quietly chipping my own flint ax, after the manner of my forefathers a few thousand years back, as be troubled with the endless malady of thought which now affects us all, for such a reward. But I venture," he asserts, "to say that such views are contrary alike to reason and to fact." Laboratories have done better things for mankind than the invention of material comforts, and I believe that one of these better things—not by any means one of the best, but still a thing well worth doing—has been to teach some, who would not otherwise have learned the lesson, the dignity of manual labor and the value of skilled labor. In plain English, a laboratory is the place for labor, a workshop. Every one who is well trained in its methods is a handicraftsman, a skilled workman.

If you were asked what workmen best show how much may be done by training to develop the latent delicacy and exactness of human fingers and human eyes, you would, no doubt, think of the engraver and the watchmaker. A watch, so well made that it tells the passing seconds through a long human life, and is as accurate after all these years as when it was new, is a wonderful example of skilled workmanship. When we reflect that technical training can give to human hands the delicacy and firmness to cut in hard steel the engraving for a treasury-note, with every line so true that a lens must be used to show the excellence of the work, it is not strange that the engraver should be selected to show what manual training can accomplish; but I hope you will not charge me with arrogance if I assert that the best examples of technical skill are to be found in scientific laboratories. In an address to workingmen, Huxley thus asserts his right to speak to his audience with authority: "The fact," he says, "is, I am, and have been any time these thirty years, a man who works with his hands—a handicraftsman. I do not," he declares, "say this in the broadly metaphorical sense in which fine gentlemen, with all the delicacy of Agag about them, trip to the hustings about election time, and protest that they too are workingmen. I really mean my words to be taken in the direct, literal and straightforward sense. In fact, if the most nimble-fingered watchmaker will come to my workshop, he may set me to put a watch together, and I will set him to dissect—say—a black beetle's nerves. I do not wish to vaunt," says Huxley, "but I am inclined to think that I shall manage my job to his satisfaction sooner than he will do his piece of work to mine. In truth, anatomy, which is my handicraft, is one of the most difficult kinds of mechanical labor, involving as it does not only lightness and dexterity of hand but sharp eyes and endless patience."

But to tear down or take to pieces is not to build up, and some who admit that the study of anatomy calls for long training may nevertheless assert that the work of the anatomist is not constructive but destructive. It is to show the error of this assertion that I ask you to listen to a short outline of a bit of constructive work of great delicacy which is carried on daily in biological laboratories. The zoologist uses many fine tools, among them the sharp-pointed dart which he dissects out from the sting of the bee, but he often needs to study complicated organisms which are too minute or too delicate for such rough implements. When he wishes to study the structure of some organism too small or too delicate for ordinary dissection, and too opaque for examination with a microscope, he cuts it up into sections or slices which, when properly prepared, will be transparent and favorable for examination with a microscope. The apparatus which he uses for this purpose is so exact that a skillful hand may, by means of it, cut sections so thin that two days, of eight hours each, are needed for cutting into sections an object an inch long, one cut and the return of the knife for the next cut being made every two seconds. If to this be added the time given to handling the delicate sections, to placing them in order, and to their preparation for examination with a microscope—work so delicate that fingers and eyes are taxed to their utmost limit—more than two weeks of uninterrupted labor must be bestowed upon an object an inch long, before it is ready to be studied, and before the real task begins.

The mere examination with a microscope of twenty or thirty thousand sections is the work of weeks, but this alone will not accomplish the purpose of the student. His aim is to gain a knowledge of the organism as a whole, as it would appear if it were enlarged as much as the section under the microscope; and he must therefore combine all the thirty thousand sections in a single view. Now, the human mind cannot grasp thirty thousand objects at one time, or directly compare them with each other, and if the student is to picture to himself the organism as it would be if all the sections were replaced in series, he must acquire the art of reconstructing, in wax or clay, or on paper, or in his mind, solid objects from transverse sections. If the master mechanic who is able to build a ship from drawings of sections and elevations is a skilled workman, no one can refuse the same name to a naturalist who thus reconstructs an organism from sections. Every one knows the practical value of the ship-builder's work, but the naturalist is often asked what reason there is for all his hard labor. I have observed, however, that they who ask why students in laboratories work so hard are commonly the very persons who assert that the higher education of our young men breeds habits of idleness, and unfits them for the serious work of life. You remember that Montaigne tells us consistency is the last thing we can expect from human beings, since he asserts that men "change as that beast that takes the color of the place wherein it is laid"; but you will, no doubt, agree that one who, while asking why students in laboratories work so hard, asserts that work in laboratories encourages idleness, does not merit the serious consideration of those who try to be consistent.

It has always been the lot of the majority of mankind to earn their bread by doing common-place, tiresome things, in common-place, tiresome ways, and if education made young men reluctant to do their duty in that state of life to which it shall please God to call them, it would be a mistake. But I do not know any way to find out what is that state of life to which a young man is called, except to give him the opportunity to train and develop all his faculties to the limit of his capacity, in order that he may discover what is that state of life in which he can do the best for himself and the most for his fellowmen. Some look upon the college with distrust because they fear that it may foster a tendency to esteem men because of some mere accident of birth, or position, or opportunity, rather than for their inherent worth. I do not feel able to say whether social rank is or is not becoming more marked among us. The problem is too difficult for me, and there seems to be much to be said on both sides; but I do not believe that the most radical of socialists sees any sign of the establishment of an aristocracy of learning. In fact, many an old-fashioned pedagogue sighs for the return of the day when the village should all declare how much he knew.

If it is true that human sympathies are growing narrow instead of broad, I do not believe that this can be laid to the door of education; for the modern university, with its scientific laboratories, seems to me to be distinctively democratic in its influence. However the case may have been with what, forty years ago, was called the education of a gentleman, it seems to me to be one of the services of the scientific laboratory, that it has taught to that part of mankind which has leisure and opportunities, that manual skill is a thing to be held in honor, both as a means for reaching mechanical results, and, still more, as a way to train the mind. One need not be very old to remember the day when it was held a baseness to write fair, or to exhibit mechanical efficiency of any sort. Even at the present day, we find, now and then, in a scientific laboratory, a young man who asserts that he cannot draw, although he quickly discovers the deficiency in his early training and seeks to correct it.

Fifty years ago many men who called themselves educated were mere untrained, undeveloped children in manual skill, and some of them were proud of their incompetency; for nothing would have more surprised them than an assertion that their inability to help themselves with their hands was a badge of ignorance, although they would, no doubt, have treated the assertion with the contempt which they thought it merited. Artists and physicians were trained workmen, but the artist was looked down upon as a Bohemian, outside the pale of good society. He was expected to receive the notice of the elect with proper humility, and, keeping himself in his place, to learn that admiration for his work gave no claim to personal respect. While the high character and sterling worth of the medical man have always won respect, his skill in the use of his hands was long held by those who were superior to any such weakness, to place him beneath the lawyer and the clergyman in the social scale. "If such a woman," says Major Pendennis, "chooses to run away with her uncle's doctor, and marry below her rank,—why, I don't think it a laughing matter, hang me if I do." Major Pendennis was an old fogy, and the world moves; for Oliver Wendell Holmes, M. D., tells us, in 1881, that "An English bishop proclaimed the fact before an assembly of physicians the other day that he was not 'ashamed to say that he had a son who was a doctor.' Very kind that was of the bishop," says Dr. Holmes, "and very proud his medical audience must have felt. Perhaps he was not ashamed of the Gospel of Luke, the beloved physician, or even of the teachings which fell from the lips of One who was a carpenter, and the son of a carpenter."

I doubt whether any one now thinks that an artist or a physician who has trained his hands and his eyes is, on this account, any less worthy of esteem and respect than one who has undertaken to educate his mind by neglecting his body. I also believe that the change is due in no small degree to the influence of laboratories; for out of the laboratory for research in pure science there has grown, on the one hand the technical school, and on the other the manual-training school and the kindergarten; while a view of the very nature of education itself which the professor of the old school would have branded as dangerous, if not positively wicked, has come to be universally accepted. The old view of education, which had come down to us from mediæval times, was that, since the body is essentially base and material, while the mind is something of a different and higher nature, so unfortunate as to be shut up for a time in a vile body, the true way to train the mind is to get at it directly, neglecting the body; although the old-fashioned pedagogue found, as a practical matter, that he could not get even the Latin grammar into the mind of a common school-boy without severely exercising a part of the boy's anatomy which

shows little fitness for improvement by exercise. There are still some, no doubt, who view with alarm as savoring of materialism, the assertion that our bodies are part of our minds, and that bodily training is mental training, although it is hard to imagine what would have been the astonishment of good Bishop Berkeley, had he been told that any one would be disquieted, well nigh two hundred years after the publication of the essay on Human Knowledge, by the conviction that the bodies which we see and feel and use, and the brains which we discover by reflection, are part of our minds. At any rate, the educational reform has come about, and the truth that bodily training is mental training has penetrated our whole educational system. A man who is unable to use his hands in the ordinary affairs of life is now considered to be, in so far, not learned but incapable, and no more worthy of honor than those ants which are so helpless that they starve to death in sight of food when they are deprived of the service of their slaves.

You will tell me, however, that while it is undoubtedly a good thing to teach a few foolish people what a little common sense should have taught them long ago, it is not a great thing. I quite agree with you. The educational reform which has been brought about by scientific laboratories is only one of their small fruits, although we could better spare some famous inventions; for, small as it is, it is an intellectual fruit, and not a mere addition to our material comforts, and I need not tell you that all the greatest services which science has rendered to mankind are intellectual services. While it is by her works that science is justified, her temple is not the patent-office but the laboratory. While first undertaken for some purpose of the sort which is commonly called practical, each advance in natural knowledge has led inevitably to profound changes in our thoughts about nature, and in our views of our own places in nature, and of the range and limits of our mind. "What," asks Huxley, "could seem wiser, from a mere material point of view, more innocent, from a theological one, to an ancient people, than that they should learn the exact succession of the seasons, as warnings for their husbandmen; or the position of the stars, as guides to their rude navigators? But what has grown out of this search for knowledge of so merely useful a character? You all know the reply; astronomy—which, of all sciences, has filled men's minds with general ideas of a character most foreign to their daily experience, and has, more than any other, rendered it impossible for them to accept the beliefs of their fathers."

What is true of astronomy is true of all the other departments of science. Their greatest and most practical results, those which have most influenced the human mind, those that mankind can least afford to spare, are intellectual results. For while each advance has seemed, at first, to lead to intellectual disaster, more mature thought and better judgment have soon led mankind to value it at its true worth, and to prize it as a permanent addition to truth; although the difficulty which we find in adjusting ourselves to new conceptions of nature, and in finding their true place in our thoughts, is perennial, for no great extension of natural knowledge ever has won, or is ever likely to win, a place for itself, without an intellectual struggle. The warfare of science has seemed to some, I regret to say even to some scientific men who ought to know better, to be a disaster, and a thing altogether to be deplored, although this does not seem at all clear to me. In fact, I doubt whether the progress of science would have been as uninterrupted and as irresistible as it has been—whether the great scientific generalizations which have done most to correct our misconceptions, and to modify human thoughts and human beliefs would have been so thoroughly analyzed, so completely stripped of all side issues and irrelevant complications, and so well reduced to that simple form which commands assent—if it were not for the natural conservatism of the human mind.

The latter years of our century have witnessed many notable struggles for the establishment of new conceptions of nature. One of the most notable has centered around the discovery, by Wallace and Darwin, that the characteristics of living things have arisen in an unending struggle for existence, in which vague and indefinite adjustments have been slowly converted into exact and definite adaptations, by the extermination of the relatively unfit and the survival of the fittest. The warfare of science seems to me to be only a part of this process of natural selection; for, as Berkeley pointed out long ago: "The work of science is to unravel our prejudices and mistakes, untwisting the closest connections, distinguishing things that are different, instead of confused and perplexed, giving us distinct views; gradually correcting our judgment, and reducing it to a philosophical exactness." If I saw any reason to believe that the coming scientific workers and thinkers are to escape from that intellectual tension which we call obstinate bigotry or enlightened earnestness, according to our point of view, I should be less sure than I am that the march of intellectual progress is to be as irresistible and as uninterrupted in the future as it has been in the past; but I fail to see any such signs. On the contrary, I do see many signs which, if I understand them, show that science is about to demand, in fact is already demanding, changes in the prevailing views of our relation to nature which will bring about an intellectual revolution, compared with which the struggles for the truths of astronomy and geology and zoology are mere skirmishes. As I also believe that this change will be brought about by the general acceptance of the definition of science which I have just quoted from Berkeley, I think we shall find profit in asking what led him to this definition. He lived in a day of great intellectual activity, for Newton's discovery that all the hosts of heaven are a vast mechanism regulated according to simple laws, had made many thoughtful men reflect that all the phenomena of nature may possibly be resolved into the movements of matter according to the laws of mechanics.

Many in Berkeley's day had thought that this view of nature leads to consequences which some looked upon with horror, while they were, no doubt, welcomed by the dissolute courtiers of George I as an excuse for cutting adrift from all the restraints of morality. It was Berkeley's great service to mankind to point out, in a wonderful essay written before his twenty-fifth year, that mechanical conceptions of nature are so far from warranting the inferences of those who, in the seventeenth century, called themselves freethinkers, as to be antagonistic to these inferences, and irreconcilable with them. Berkeley is as thoroughly convinced as any freethinker that all the phenomena in nature are produced by motion; that they

conform to mechanical laws; that the universe and everything in it is a vast machine; but he calls upon the freethinker to examine and find out what he means by a machine, and he points out, as Aristotle had done before him, that a natural law is not a cause, or an agent who does things, but a general rule which teaches us how to act and what to expect. He shows us that we know nothing about matter and motion except what we see and feel and perceive by our senses and discover by reflection; but since perception and reflection are states of mind, it is clear that we cannot perceive or reflect upon anything except what is in our minds, and that the only existence we know anything about is mental existence; for the things I see and feel are my states of consciousness, and the existence of a state of consciousness apart from a thinking mind is a contradiction. "Some truths there are," says Berkeley, "so near and obvious to the mind that a man need only open his eyes to see them. Such I take this important one to be, viz.: That all the choir of heaven and furniture of earth—in a word, all those bodies that compose the mighty frame of the world—have not any substance without a mind; that their being is to be perceived or known."

Some who have never taken the trouble to read Berkeley assert that he teaches that the external world is only a creation of our own minds, or a dream; but this is a gross caricature, for he shows, in a series of beautiful essays and dialogues, by reasoning in which no one has ever found any serious flaw, that while the external world is real beyond the possibility of doubt, its reality is the reality of language, and that nature is a language by which we are entertained and instructed and delighted, and that when we use such phrases as "the language of nature," and "the interpretation of nature," our words are not figurative, but literal. He shows that each event is, in course of nature, a sign of others that may be expected, and that the work of science is to teach us the significance of natural signs, that we may understand things which mean nothing to the ignorant. "As the natural connection of signs with the things signified is regular and constant, it forms a sort of rational discourse. Therefore," he tells us, "the phenomena of nature, which strike on the senses, and are understood by the mind, do form not only a magnificent spectacle, but also a most coherent, entertaining discourse; and to effect this they are conducted, ranged, and adjusted by the greatest wisdom. This language or discourse is studied with different attention, and interpreted with different degrees of skill. But so far as men have studied and remarked its rules, and can interpret right, they are said to be knowing in nature."

Now, language, being an exchange of ideas, implies both a recipient mind and an originating mind; and Berkeley tells us, therefore, "that, setting aside all help of astronomy and natural philosophy, all contemplation of the contrivance, order, and adjustment of things, the bare existence of the sensible world is evidence of a creative mind, because the sensible world is a language. Our way to find out things is not to try to deduce them from mechanical principles, or principles of any sort, with the philosophers, but to listen humbly to the language of nature, as the true men of science always have done. Our part is not active but passive, and so far as we listen attentively and strive to understand, we shall make no mistakes. If, however, we are not makers of natural knowledge, but listeners, it follows that the work of science is not to add to knowledge, but to "unravel our prejudices and mistakes, untwisting the closest connections, distinguishing things that are different, instead of confused and perplexed, giving us distinct views; gradually correcting our judgment, and reducing it to a philosophical exactness." But the correction of our natural responses, and their reduction to exactness, by the suppression of those that are confused and perplexed, and the preservation of those that are definite and distinct, and ultimately by the extinction of the deluded minds and the survival of those that are sane, is what I understand by natural selection. Just so far as natural selection is a mechanical explanation of the origin of species, just so far is it also a mechanical explanation of natural knowledge.

The most practical and important question which rational human beings can ask is how we may distinguish truth from error, in order that we may be sure about our actions and rightly order our lives; and the greatest service of Charles Darwin to the intellectual life of mankind is that he has led us to ask whether we may not, some time, find a mechanical explanation of that rational judgment which is innate in human minds; whether this may not itself be part of the physical order of nature; whether those judgments which we call errors may not be the ones which lead us into danger and tend to our destruction; whether it may not be because a judgment has proved beneficial in the struggle for existence, that we call it true; whether language itself, even the most rational discourse, may not be a natural phenomenon which lies entirely within the chain of physical causation. All are now familiar with the work of the physiologists in localizing functions of the brain. Every one knows that mental diseases may often be traced to specific pathological causes. The psychologists are occupied in tracing the transformation of the simple, responsive actions of the lower animals and of human infants into the rational actions of man, by a process of gradual correction and adjustment. The philologist, who studies the life and growth of language, tells us that this, too, exhibits mechanical law. From all these sources, and from many others, evidence is accumulating which leads many thoughtful men to believe that the progress of natural knowledge is giving us a physical explanation of mind; that we are making rapid strides towards the discovery of a mechanical equivalent of truth; and that all that choir of heaven and furniture of the earth which we perceive by our senses and discover by reflection, may be no more than one who knows the whole natural history of our bodily frames might have expected.

Now I need not warn those scientific men who will have the task of assuring mankind that these novel conceptions are not pernicious, but wholesome, that their work will be neither light nor easy, although I believe that if Berkeley could revisit us, he would, with a kindly smile, reassure those who find it difficult to reconcile mechanical conceptions of mind with belief in our moral responsibility and in the value of our reason; that he would remind them that mechanical principles are not agents who do things, nor rulers and governors over nature, but only general rules which teach us how to act and what to expect. I imagine he would remind us that our way

to find out things is not to deduce them from mechanical principles, or logical principles, or philosophical principles, or principles of any sort, but to listen to the language of nature. They who are disquieted by the conviction that there is only one kind of knowledge, and but one way to acquire it, should reflect that the scientific method of acquiring knowledge is to listen to the language of nature; and that proof that the scientific method is adequate to all our needs, is proof that this language is adequate to all our needs.

As I understand Berkeley, it is not because nature is a language that he holds it to be intended; but because the language of nature is useful, and instructive, and delightful to hear. Even if we see reason to ask whether this language may not be mechanical and explicable by physical science, I fail to see why we should challenge Berkeley's belief that it is intended, unless we doubt whether the language of nature is useful, and profitable, and delightful. Does any man of science doubt whether the words "language of nature," and "interpretation of nature," are used with clear, intelligible meaning? Is not the question whether nature is a language, which we hear to our delight and profit and instruction, quite a different matter from the question whether the language of nature is or is not mechanical? He who fears that the discovery of mechanical explanations of the language of nature would destroy the proof that nature is a language, seems no more reasonable than one who, having enjoyed and profited by good books, should assert that these books have lost their use and their power to please and to instruct, through the discovery that they were made by machinery in printing-offices.

The man of science should be the last to doubt the value of this language, even for an instant; for he asserts that it is because exact science does help one walk with sure feet where others grope and stumble, that the promotion of natural knowledge is both the greatest of all pleasures and the first and highest of duties. How can one who knows that natural knowledge does correct our judgment, and help us to avoid the dangers that beset and destroy the ignorant, ask whether nature is a language, profitable to direct? "The attitude of modern science is erect; her aspect serene; her determination inexorable; her onward march unflinching; because she believes herself, in the order of Providence, the true successor of those men of old who brought down the light of heaven to men. Humility may be taken for granted as existing in every sane human being; but it may be that it most truly manifests itself to-day in the readiness with which we bow to new truths, as they come from the scholars, the teachers, to whom the inspiration of the Almighty giveth understanding."

THE TEACHING OF PSYCHIATRY.*

By Henry M. Hurd, M. D., *Superintendent The Johns Hopkins Hospital and Professor of Psychiatry, Johns Hopkins University.*

Psychiatry has hardly emerged from the swaddling bands of metaphysics, dogma and tradition. Insanity is no longer considered demoniacal possession, but the terminology of psychiatry is still encumbered with terms which are no less misleading and out of date than were the terms employed a century ago to describe the conditions of ordinary disease. Such a terminology denoting erroneous conceptions of the character of insanity needs to be replaced by a better—or at least by one more consistent with modern knowledge. The old and new are not yet welded together into a harmonious science. Psychiatry once an art only is a new science, if indeed it may even now be considered to have attained to that dignity. If it is a science, it is still in the process of growth and development and has not attained its majority. There are recorded many observations of mental disease, and much clinical work has been done during the past century, but the master mind who is to bring these isolated facts together and weave them into a framework of law has not yet appeared. This work remains to be initiated by one who has the time and leisure to make an exhaustive study of facts covering a period of years and to combine them together in such fashion as may give a conception of mental disease as a whole—such a work as was accomplished by Louis for typhoid fever, pneumonia and tuberculosis. How did he accomplish this? Let me quote in answer from his friend and disciple, James Jackson. "Returning to France at the age of thirty-two, he (Louis) was about to engage in private practice. He was then led to examine anew the state of the science of medicine, and was dissatisfied with it. He now decided to abandon the thoughts of practice for a time, and to devote himself to observation; that is, to the study of disease as it actually presents itself. With this view he went into the Hospital La Charité in Paris, and followed the practice of M. Chomel, now a physician at the Hotel Dieu and professor of clinical medicine, and highly esteemed as an author. M. Louis passed nearly seven years in studying medicine in this way. The first part of this time he was learning how to make observations. When he thought he had attained this art, he threw away, as I have understood, the notes he had already collected, and began anew to accumulate exact observations of the phenomena presented by the sick and of those derived from an examination after death in the fatal cases. In this course of observations he did not make a selection of cases, but took them as they were presented, indiscriminately. He was not in a hurry to make deductions from his cases, satisfied that he was gathering the materials, from which truth must ultimately be elicited. He was only careful that his observations should be correct, and had not any general principles, or doctrines, for which he sought support or confirmation.

"To estimate the value of his observations it is necessary to understand the plan on which he collected them. First, then he ascertained when the patient under his examinations began

* A portion of the Presidential Address at the Annual Meeting of the American Medico-Psychological Association in New York, May, 1899.

to be diseased. Not satisfied with vague answers, he went back to the period when the patient enjoyed his usual health; and he also endeavored to learn whether that usual health had been firm, or in any respect infirm. He noted also the age, occupation, residence and manner of living of the patient; likewise any accident which had occurred, and which might have influenced the disease then affecting him. He ascertained also, as much as possible, the diseases which had occurred in the family of his patient. Secondly, he inquired into the present disease, ascertaining not only what symptoms had marked its commencement, but those which had been subsequently developed and the order of their occurrence; and recording those which might not seem to be connected with the principal disease, as well as those which were so connected; also, measuring the degree or violence of each symptom with as much accuracy as the case would admit. Thirdly, he noted the actual phenomena present at his examination, depending for this not only on the statement of the patient, but on his own senses, his eyes, his ears and his hands. Under this and the preceding head he was not satisfied with noting the functions in which the patient complained of disorder, but examined carefully as to all the functions, recording their state as being healthy or otherwise, and even noticing the absence of symptoms which might bear on the diagnosis. Thus all secondary diseases, and those which accidentally coexisted with the principal malady, were brought under his view. Fourthly, he continued to watch his patient from day to day, carefully recording all the changes which occurred to him till his restoration to health or his decease. Fifthly, in the fatal cases he exercised the same scrupulous care in examining the dead, as he had in regard to the living subject. Prepared by a minute acquaintance with anatomy, and familiar with the changes wrought by disease, he looked not only at the parts where the principal disorder was manifested, but at all the organs. His notes did not state opinions, but facts. He recorded in regard to each part, which was not quite healthy in its appearance, the changes in color, consistence, firmness, thickness, etc.; not contenting himself with saying that a part was inflamed, or was cancerous, or with the use of any general but indefinite terms."

In this matter Louis was able to differentiate diseases like typhus and typhoid—which had formerly been confounded—and tuberculosis and pneumonia, and to settle certain general principles which will endure as long as medicine is known as a science. Such a work needs to be done with the various forms of insanity, so that we may know their physical laws and underlying conditions.

The period of vague description and unsatisfactory, because stereotyped, case-books is drawing to a close, and precise definition and numerical methods should take their place. One would think that with the present perfect organization of hospitals for the insane it would even now be possible to ascertain certain facts with great certainty. Take, for example, the oft-repeated statement regarding paretic dementia, that it is increasing, that women are increasingly victims of the disorder, and that the ambitious form is surely disappearing and is replaced by the demented form. Who knows with certainty as to the correctness of these assertions and who possesses the data for a satisfactory reply to the query? If, however, any method of inquiry, rivaling in accuracy and completeness Louis' numerical method, existed in our hospitals for the insane, how readily such questions could be answered. Many years ago, Sir James Crichton Browne published a most suggestive paper entitled a "Plea for the more Minute Study of Mania," in which he spoke of the desirability of investigating the areas of the cerebral cortex involved in mania in the light of the muscular movements characterizing the maniacal frenzy. The method suggested was most helpful by foreshadowing new methods of investigation and threw much light upon the relations of insane manifestations to morbid brain conditions. An equally interesting study might be made of other insane states, but as yet no one has attempted it. They all deserve painstaking and detailed study. The objection, however, is made to such clinical studies of mental disease that they do not explain mental phenomena and that it is impossible to connect mental manifestations with physical conditions. Mental phenomena, it is said, cannot be weighed and measured; they are evanescent and fleeting and cannot be reduced to grams or grains or measured by instruments of precision. They can be described as emotional states, modes of thought, sense impressions and intellectual judgments. You cannot recognize an emotion by its color or a thought by its outward appearance. Auscultation does not reveal mental processes, nor does the microscope or the aniline dye give any clue to their presence or absence. It might be said with equal correctness that no process yet exists which will determine the difference between a dead or living cell or the complex set of bodily processes which we know as vitality. We can not explain these phenomena but we can deal with them as we would with any other known facts; they are clinical findings and we should seek to know the laws of their normal and morbid manifestations, even if we do not know wherein their vitality resides or the process of its dissolution in death. Until vital processes, which are vastly more appreciable than mental processes, are known and satisfactorily demonstrated it is unjust to charge the alienist with a lack of scientific precision because he does not explain the physical basis of mental action and the conditions of its exercise. The alienist can observe facts, analyze symptoms, record normal and abnormal mental manifestations and seek for the law of their being. This line of careful study is open to all earnest clinicians.

Morbid mental manifestations can also be recorded as mental phenomena in terms intelligent to all students of psychiatry. Their underlying physical basis can sometimes be determined by known methods of investigation. Chemical, bacteriological and clinical methods are all applicable to these investigations. Internal medicine, neurology, surgery and gynecology assist in revealing the morbid process which has given rise to the aberrant mental manifestation. The body metabolism can be studied by physiological chemistry; the physiology of secretion and excretion gives valuable hints; and nerve tire, fatigue effects, reaction time and other phenomena elicited by the methods of psychology throw a flood of light upon neurasthenic and anæmic conditions. But beside and beyond these comes the investigation of phenomena which must be studied by methods peculiar to mental disease, for

which at present we are but inadequately equipped and for a better knowledge of which we must look to the newly organized pathological laboratories which are springing up throughout the United States. To two of these, that of New York, presided over by Dr. Van Gieson, and that at the McLean Hospital, under the able guidance of Dr. Cowles (I mention these specially in no invidious spirit towards others, but simply because I know more of their work—all doubtless deserve equal praise)—to these two laboratories, I repeat, we look for new methods and substantial discoveries. Their utility at first, however, must be confined to those who are familiar with the methods of research work. The superstructure of medical knowledge has been reared slowly and almost imperceptibly by the acquisition of isolated facts which are gathered painstakingly into a confused heap by a multitude of observers ready for the hand of a master-builder, like Virchow with his cellular pathology, or Pasteur with his study of infective processes, or Koch with his bacteria. These research workers must devise new methods far exceeding in delicacy and precision those required by other branches of medicine. Here the workers must have special training and must hew their way through an unbroken forest of facts often without guide or compass. May no one be so unwise as to require a harvest before the ground is cleared and made ready for the seed. All praise to the commissioners in lunacy of this noble State who have had the courage to initiate this great movement and a far-seeing sagacity in the selection of the means to attain success.

I now approach the question of the best method of teaching this most difficult of the branches of medicine, and I think all will agree with von Jaksch's statement before the Congress of Internal Medicine in April last that: "Only one specialty must the student go to the specialist for, and that is mental disease. The importance of this has become so clear in the last few years, the experience required for its proper teaching is of such a special character and yet a knowledge of it is so indispensable, that a special professorship in it is always needed and the study of it should be made obligatory."

In view of the difficulties of the subject and the necessity of a thorough training in all subsidiary branches of medicine, it seems imperative that instruction in psychiatry should be placed in the last year of the medical course. At this time the student will have had a full training in psychology, neurology, physiological chemistry, bacteriology and clinical medicine. When he is ready for this study he should have a review of neurology in its relations to mental disorder. The precision of neurology offers an excellent introduction to psychiatry, and its methods should be transferred to the latter study as far as possible. A word of caution, however, may not be inappropriate. The methods of neurology are inadequate to the interpretation of many of the phenomena of mental disease and an attempt to confine the study wholly to neurological data omits many most important details of mental disease. Hence neurology and its methods, while most valuable, can only serve as an introduction. The futility of depending upon neurology for all the methods of investigation has well been pointed out by Van Gieson in his most suggestive paper on "The Correlation of Sciences in the Investigation of Nervous and Mental Diseases." The special study of the nervous system as connected with insanity should lead up to a careful study of all insane conditions and special forms of disease. This, in my judgment, should be from a text book or from carefully prepared lectures supplemented by clinical demonstrations of the different forms. These should be supplied by institutions designed for the treatment of acute insanities, and insane patients should be seen and studied until the student has acquired a familiarity with them.* It is much to be regretted that many of the best institutions for the custody and treatment of the insane are situated so far from centers for medical teaching as to preclude their use as adjuncts of medical schools. It seems of little real utility to introduce students into the wards of a hospital for the insane two or three times a year. The student should see the various phases of insanity frequently, and thus, by watching their development, become thoroughly familiar with them. It is to be hoped that there will grow up in every city a detention hospital—not a detention ward but a well-organized hospital—with facilities for classification, for the reception of all cases of insanity in the dependent or semi-dependent classes, to which could be sent all recent cases of insanity for observation and study. Some of these patients, being cases of ephemeral excitement or of delirium or alcoholic or habit cases might soon regain self-control and return home without being committed to institutions for the insane at all. The majority, however, would probably require to be transferred to such institutions. Meantime, while under observation and while their symptoms were being studied with a view to their final disposition, they could be utilized for medical instruction precisely like any patients in general hospitals. Those who are connected with hospitals for the insane have often been distressed by the commitment of hysterical, neurasthenic and other improper patients who, had a detention hospital been provided, might have been treated according to general hospital methods and sent to their homes without the stigma of a commitment to a hospital for the insane as insane and irresponsible persons. In the same connection, I would urge the importance of providing at every general hospital an out-patient department for the treatment of cases of insanity by alienists rather than by neurologists. I regard such departments as most important adjuncts to the successful and useful treatment of psychiatry. I am persuaded that many neurasthenic, anæmic or melancholic cases might thus be seen

*In this connection I would call attention to the method adopted by one of our most successful teachers of psychiatry, Dr. Cowles, of Harvard University. In a recent letter he presents a syllabus of his course, which covers in order Imperative Conceptions and Obsessions; the Laws of Nervous and Mental Mechanism; an Analysis of the Mental Symptoms of Nervous Exhaustion and of the Acute Psychoses, of the Essential Dementias, and of Organic and Degenerative Psychoses. He adds: "These indicate my conception of a method of teaching psychiatry, in which the guiding purpose is to put the student in posession of principles with a sufficient illustration by cases to make them clear. This method of teaching principles seems the better one for students taking up newly this subject."

and treated in the beginning of their disorders and cured without needing to resort to the hospital for the insane. Under present methods, however, the condition of such patients is not promptly recognized and they eventually come to the hospital for the insane at a stage of their disease which is not as favorable for cure. For a number of years I observed such a clinic in the out-patient department at the Johns Hopkins Hospital and was favorably impressed by its practical utility. Not the least of such utility is the opportunity which such a clinic affords for the instruction of medical students. I am convinced that there are several forms of mental disease which the alienist physician rarely or never sees in their early stages because the mental symptoms are not grave enough to justify the important and hazardous step of commitment to institutions. The medical student, however, should see them, because of the probability that his attention will be called to them when he enters upon medical practice. By the study of the symptoms of these patients under the guidance of the alienist physician the student becomes familiar with the proper investigation of mental cases and acquires an ability to win their confidence, to understand their morbid mental condition and to treat them rationally. An experience of several years in the general hospital has convinced me that neurasthenic and mental cases form an important part of those cases which physicians in general practice are called upon to treat. No medical teaching can be considered thorough or complete which does not furnish the student adequate clinical experience with such cases. The same is true of the training of nurses. Every well-trained nurse should have had experience in the care of mental cases. In no other manner can the student acquire a familiarity with the appearances of early mental disease. I am glad to be able to add that such a clinic has existed for some years in connection with the Pennsylvania Hospital and a similar one has recently been organized in Boston. I look forward to the time when every hospital which furnishes facilities for medical teaching will provide similar clinics for out-patients. I would emphasize most strongly the need of the study of insanity in its clinical forms by clinical methods, not to support preconceived theories or to reconcile seemingly inconsistent facts. We have a disease to deal with which is slow in its onset, protean in its manifestations, chronic in its course and which if uncured ends in dementia and mental death. What are its causes, the immediate exciting factor in its outburst, the order of its manifestations and development and the physical and mental phenomena characteristic of the entire course of the disease? As soon as these facts are ascertained and arranged and the pathological findings are studied in connection with the clinical history and in the light of the disease as a whole, I am sure that a rational explanation will be found for insane conditions and a line of treatment evolved which may increase our hopes of cure. Until this is done I have little expectation that any theory, however plausible, or any flight of the imagination, however brilliant will suffice to give us the clue. If the theory of a retraction of the processes of the neuron had a particle of evidence behind it we might explain some of these phenomena, but in the light of our present knowledge it seems worse than futile to depend upon it for a final explanation of diseased processes. Medical science is a structure the building stones of which are isolated facts, which have been fitted together with infinite pains and after many errors and blunders. Many of the stones after lying in position for years and even centuries have been found wrongly shaped and have been removed from the wall to the great detriment of the superstructure. The aggregation of truth which constitutes the science of medicine has been slowly and painstakingly made and much has needed to be done over. If science were a growth from some great vivifying germinal truth, we might found it upon a brilliant theory or an illuminating generalization. Unfortunately, it is not an organic but a composite product. It does not grow like an oak from an acorn; it is not the logical result of *a priori* processes; it yields its truths to no open sesame; it knows no philosopher's stone by which theory can be transmuted into priceless truth; it is simply a collection of facts with deductions therefrom.

When the student has become familiar with the clinical features of ordinary insanity he should have an opportunity to recognize its terminal forms in large institutions for the chronic insane and an added opportunity to study the pathology of the disease. Afterwards, should come instruction in medical jurisprudence and in the varied relations of the insane to the law, the State and to society in general. Less than the course above outlined should not be thought of and more would not come amiss. It is gratifying to observe a growing tendency on the part of medical schools to furnish this instruction. I believe, however, if the minimum of requirements which I have outlined could be exacted in every medical school, we would find a growing interest in psychiatry and an increased willingness on the part of men of the first class to enter lunacy practice or to become connected with institutions for the care and treatment of the insane.

Thus much for the teaching of psychiatry to the general practitioner and to the ordinary student of medicine. The training of teachers and of experts in mental disease should, however, go far beyond what I have outlined.

For these, opportunities for special graduate study should be afforded at some one of the great medical centers of the United States, and preferably in connection with one of the Pathological Institutes. Here a training should be given in psychology and its methods of studying normal and abnormal processes. Anthropology should also be pursued to give a knowledge of the inheritances of the race and the characteristics of races and peoples, their modes of development, their folk-lore traditions and inherited beliefs. In passing, I would remark that in my judgment the careful study of this unwritten tradition which has been handed down from generation to generation, surviving both barbarism and civilization so-called, would throw much light upon the development of delusions and other manifestations of insanity. Many problems of heredity are best solved by the methods of anthropological study, as also the relations between degeneracy, criminality and insanity. Pathology and histology should also receive careful consideration, and neuropathology should be pursued to throw light upon the nutrition of the nerve-cells and their

relation to poisons from within and without. These and kindred studies are of the highest interest, and should engage the best minds of the medical profession. The soil to be tilled has long lain fallow, but the harvest now should not long be delayed. The future of psychiatry is inspiring and full of promise.

A NEW APPARATUS DESIGNED FOR THE SUPPORT AND SAFE ANAESTHETIZATION OF PATIENTS WHILE IN THE KNEE-CHEST POSITION.*

By Clement A. Penrose, M. D.

IMPORTANCE OF THE KNEE-CHEST POSITION.

In the recent publication of Dr. Howard Kelly's magnificent work on operative gynaecology, the importance of the knee-chest position in the surgery of the bladder and rectum, is so thoroughly established that it is hardly necessary to emphazise it here other than very briefly. No other position allows of such complete expansion of these organs, thereby facilitating their examination, topical treatment and surgery. In this position, without difficulty, the entire mucous membranes of both bladder and rectum by means of headlight and speculum can be explored, areas of disease treated or removed, and the ureters catheterized, to determine their exact location as a preliminary in a complete hysterectomy, to drain and irrigate the kidneys, or to locate renal calculi with wax-tipped catheters, etc., etc.

NECESSITY FOR ANAESTHESIA IN THE KNEE-CHEST POSITION.

Although of great service in a great number of instances without an anaesthetic, yet in a majority of cases anaesthesia is necessary to thoroughly relax the walls of bladder or rectum, to eliminate pain which is often extreme, as a preliminary to operations requiring an anaesthetic, in which case it is better, especially in nervous subjects, to do the whole under the one anaesthetization, and lastly, to relieve the feelings of the patient from the standpoint of modesty.

OBJECTIONS TO ANAESTHESIA IN THE KNEE-CHEST POSITION.

When supported in the old fashion without apparatus, the patient with weight thrown on the chest and neck bent at right angles often becomes cyanosed, breathes with great difficulty, has a high pulse, and occasionally almost suffers collapse, especially if operations are at all protracted. The anaesthetizer holding a cone with one hand and supporting the patient's head with the other, has great difficulty in holding the jaw properly forward, and in keeping track of the pulse, and in fact, never feeling quite sure of his patient's condition or stage of anaesthetization. Two assistants, one on each side, are necessary, in addition to the anaesthetizer and a man to hand instruments, to support the patient in a correct position. In spite of such support, there is yet considerable mobility, the effort to control which is very tiresome for the assistants, and disastrous to delicate manipulation.

REQUIREMENTS OF AN APPARATUS TO SUPPORT A PATIENT WHILE ANAESTHETIZED IN THE KNEE-CHEST POSITION.

1. One which allows of complete expansion of the bladder and rectum, specially the former; i. e., there being nothing in any way pressing on these parts as straps, supports, etc.
2. One which supports the chest and head in such a manner that breathing is not difficult and an anaesthetic is easily administered.
3. One which holds the patient absolutely immobile in the correct position without strain or any undue pressure, thus dispensing with an unnecessary number of assistants.
4. One which admits of patients being lifted on and off the table without difficulty or danger, while under the influence of the anaesthetic.
5. One which can be adjusted to various sizes of patients.
6. One which is not too elaborate or expensive.

That necessity is the mother of invention was possibly never more thoroughly demonstrated than in the motives which induced me to construct my apparatus. Any one who has had experience in the anaesthetization of patients while in the knee-chest position will appreciate in full the trials and tribulations of the anaesthetizer, as often in spite of the utmost care, his patients will become cyanotic and have a high pulse, and not infrequently operations are suspended owing to the sudden cessation of breathing and artificial respiration is required before they can be resumed, if completed at all. While in the service of Dr. Kelly I etherized a great number of patients in this position, and though never being so unfortunate as to lose one, had enough mental perturbation in several instances to induce me to speculate on some means by which an anaesthetic could be administered to patients in this position without additional danger. Encouraged by Dr. Kelly, who kindly offered me every facility for experimentation, I made in the summer of 1897 a crude apparatus of wood which in its essential features resembled the one now reported. This was used constantly and with gratifying success. A number of patients, twenty-five or thirty, in the course of a few months were etherized and placed on this apparatus, and among this number not one took the anaesthetic badly, nor was it necessary in a single case to hasten or bring operations to a close, owing to the condition of the patients, who, in fact were kept a much longer time on my apparatus, in several instances one half hour or more, than when held up by assistants after the old fashion. The apparatus presented to the Society this evening, consisting principally of steel, has been in constant use in the Gynaecological Department of the Johns

* Read before the Medical Society of the Johns Hopkins Hospital, January 23rd, 1899.

Hopkins Hospital for over one year, and I understand has given great satisfaction.

In light of these most encouraging results and of the increasing importance of the knee-chest position in surgery, it may safely be predicted that if by its use the chief element of danger be eliminated, i. e., the administration of the anaesthetic, major operations on the bladder and rectum of several hours' duration may be performed. Day by day the importance of certain procedures in the knee-chest position, both from a diagnostic and curative standpoint is becoming more manifest, and necessarily an apparatus which furthers such manipulation is of the utmost importance to humanity.

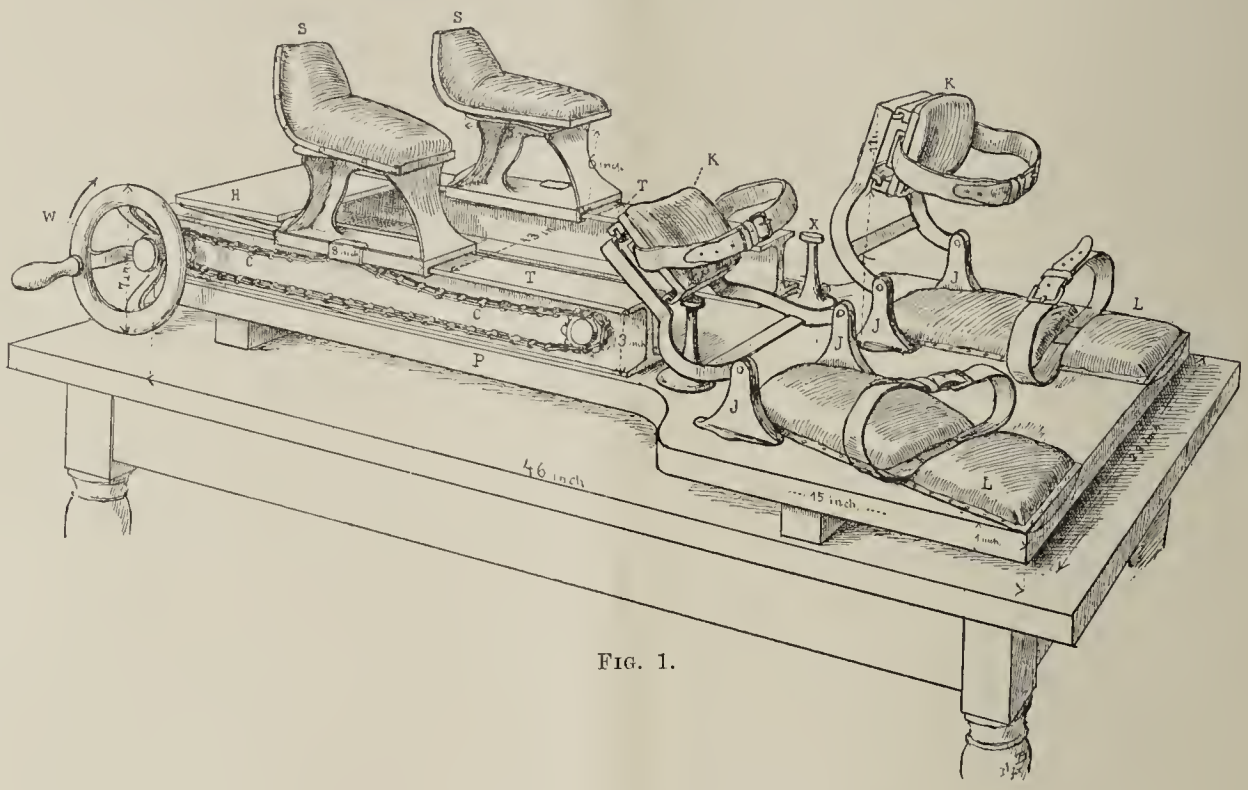


Fig. 1.

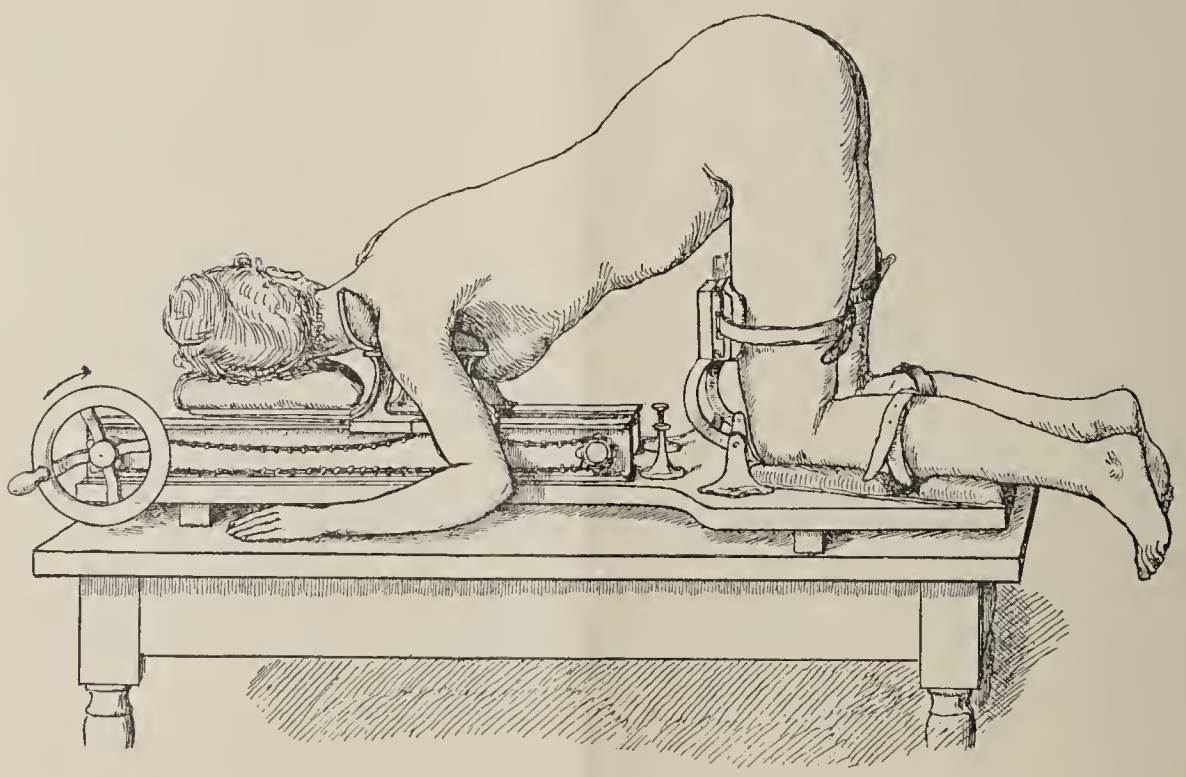


Fig. 2.

The careful drawings made for me by Mr. H. Becker, are exact representations of my apparatus without and with a patient in position. (See Figures No. 1 and 2.)

In Figure 1, the exact measurements of the apparatus are given, and a very good idea of its construction, which is exceedingly simple, and its ease of adjustment. In brief, it consists of two shoulder supports, S, S, with cushions of leather which can be moved sidewise by a screw in front, not shown in the figure, to accommodate varying widths of shoulders. These supports run on a track, T, T, being connected with a chain, C, C, which is moved by a wheel, W. A ratchet wheel with a pall on the inner side of wheel, W, not

shown in the figures, allows only of rotation in the direction of the arrow, unless the pall is released. K, K are supports which press against the front of the thigh, the cushions of which also have a motion sidewise and are held firmly in place by straps. J, J are joints corresponding to those of the knee; L, L are cushions on which the tibiae rest, with straps passing over the calves of the legs.

Figure 2, shows the patient pushed up into the correct knee-chest position. She has first been etherized on a bed or stretcher until completely relaxed. The apparatus placed on a table made especially for the purpose, and at a height desired by the operator, is then adjusted to accomodate the size of the patient. As a rule the same adjustment works for most patients unless they are very large or small. She is then lifted up and placed face downward on the apparatus, the shoulder pieces supporting the shoulders, the body being only slightly flexed. The thighs and calves are then strapped with the straps firmly to their respective cushions, and the pall being thrown on to the small ratchet wheel, the large wheel W is turned in the direction of the arrow and the patient is slowly pushed up into the correct position. A cushion can be placed on the head piece, H, which is connected to the shoulder supports, S, S, but can be detached in a moment, giving ample room between the tracks for swabbing out the mouth, holding the jaw forward, etc., etc. With the head turned slightly to one side, the anaesthetic is administered as easily as when on the back, the chest has free room for expansion between the shoulder supports, which keeping the shoulders well back are an assistance rather than otherwise to deep inspiration. The abdomen, hanging pendulous and unsupported, admits of full dilatation of both bladder and rectum with atmospheric air. Sheets, towels, etc., are readily draped in such a manner that parts for examination or operation alone are exposed.

In conclusion I would like to say that owing to the great number of patients in the surgical clinics of our large hospitals, there is a tendency to discard what may take up precious time. All experienced anaesthetizers know how much better a patient takes an anaesthetic who at first has been given it slowly with words of encouragement and suggestion spoken here and there, than those who have been badly frightened by having a cone clapped down over the face and the anaesthetic forced before becoming unconscious. The desire to save time, unfortunately among the less experienced, has made the term "a quick anaesthetizer," a synonym for a good anaesthetizer, whereas the proper and only just criterion should be the condition of the patients during the operation, when returned to the ward, and lastly, the opinion the patients have of the anaesthetizer. The conditions favoring the prolongation of the period of anaesthesia are as important as those which are desirable when a patient is going under the anaesthetic. It does take a few moments longer to place patients correctly on my apparatus than to lift them up and support them in the knee-chest position by main strength, and I might add, in many cases with awkwardness. One or two minutes are well lost if our patients run less risk, and much time is eventually saved by not having recourse later to strychnia, salt infusion, artificial respiration, etc., after operations are begun.

If placed properly on this apparatus, I feel certain that patients can be kept under an anaesthetic for as long a time in the knee-chest as in the Trendelenburg position. As but one assistant in addition to the anaesthetizer is required, the others formerly employed may be utilized in getting other cases ready for operation, etc., and thus save time.

The utility of this apparatus having been already tested for over one year in Dr. Kelly's clinics, and in many cases, I feel a much greater confidence in recommending it to those using the knee-chest position for examination or surgery.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

A Case of Hemochromatosis. Dr. Opie.

The patient, a man aged 55 years, was apparently in good health until about six weeks before his death, when he was taken with symptoms of typhoid fever. When seen two weeks later, rose-spots were well marked over the abdomen, and there was elevation of temperature and extreme weakness, a most striking feature being the extreme pigmentation of the skin, which was of a brownish color and most marked about the nipples, genital organs and the backs of the hands, strongly suggesting Addison's disease. The urine at no time showed sugar, the first examination being made about four weeks before death, and, subsequently, on several occasions, the last about three days before death. The autopsy was performed about nine hours after death. The body was that of a very much emaciated man, with pigmentation extremely well marked. On opening the abdomen there was found pigmentation of the parietal peritoneum; the liver was cirrhotic and presented a marked brownish pigmented appearance; the pleural cavities showed no evidence of inflammation; the heart was sound and not increased in size, the muscle having a yellowish-brown color; the lungs were normal, except for bronchopneumonic areas; the spleen was enlarged and very soft, with no evidence of any extreme pigmentation. The gastrointestinal tract showed extreme pigmentation more marked in the duodenum and stomach than in the ileum and jejunum, but again there was well-marked pigmentation in the large intestine. The pancreas, of a chocolate-brown color, showed thickening of the capsule and septa extending into the organ. The adrenals were of normal size and showed nothing abnormal. The kidneys were not markedly pigmented, but somewhat cloudy. The lymph glands throughout the abdomen were enlarged and presented a very brilliant brownish orange-yellow appearance. In the lower part of the ileum there were ulcers with clean bases confined particularly to the Peyer's patches. Cultures made from the heart's blood showed pure typhoid bacillus, which was also present in the liver and

gall-bladder, with lactis aerogenes in the lungs and kidneys, and colon bacillus in the pancreas.

The case, then, was one of typhoid fever, with pigmentation of the various organs, notably the liver, pancreas, heart and gastrointestinal tract, associated with cirrhosis of the liver and chronic interstitial pancreatitis.

Bands of connective tissue separated the liver lobules one from the other, and there was slight invasion of the periphery of the lobules. From the central vein bands of connective tissue extended between the columns of liver cells. The most striking feature was the abundant deposit of pigment throughout the tissue. Occasionally the whole cell body is filled with pigment, and in the most extreme cases there is evidence of cell-degeneration; the nucleus becomes shriveled and loses its staining properties, becomes very pale and finally disappears, leaving a clump of granules, still retaining the outline of the cell. This pigment, when treated with ferrocyanide of potassium and hydrochloric acid, gives the Berlin blue reaction, characteristic of iron.

In addition, there is a second form of pigment which gives no iron reaction. It is in the form of small granules of brighter yellow color, and is deposited in the smooth muscle cells of the blood-vessel walls, particularly the portal vein, and in the connective-tissue cells in the sheath of the vessels.

Iron-containing and iron-free pigment was also present in sections of the pancreas, while in the heart the iron-containing pigment was present in great quantity in the muscle cells. In the gastrointestinal canal the iron-containing pigment was present in small quantities, but the iron-free pigment in great quantities, in either the smooth muscle cells or in the connective-tissue cells. The greatest quantity in the stomach was deposited in the most internal portion of the circular layer. Other organs showed a less degree of pigmentation. In the lungs, here and there, were found connective-tissue cells which contained the iron-containing pigment. In the lymph glands was found a great quantity of the iron-containing variety, which was present in the form of extracellular globules of varied size, the pigment almost entirely replacing the gland substance, very few of the lymph cells being seen. The case then shows throughout the internal organs a deposit of two forms of pigment. Within the gland cells, notably in the liver, pancreas and heart muscle cells, there is the iron-containing pigment, while in the smooth muscle cells of the blood-vessels and the gastro intestinal canal, as well as in certain connective-tissue cells, there is a deposition of the iron-free pigment.

Under the designation "haemochromatosis" Von Recklinghausen, in 1889, described a condition of macroscopic pigmentation of various organs due to the presence in the tissues of a brown pigment derived, he thought, from the haemoglobin of the blood. An iron-containing and an iron-free pigment were found in situations corresponding to those cited in the foregoing case; cirrhosis of the liver was present. Other writers have subsequently described cases of haemochromatosis. A condition of pigment accumulation in the internal organs associated with diabetes and hypertrophic cirrhosis of the liver has been studied particularly by French writers, who on account of the well marked skin pigmentation usually present have given it the name "diabète bronzé." While in many of the early cases an iron-free pigment, being less conspicuous than the iron-containing variety, was overlooked, in several more recent both varieties have been found and their location has been that characteristic of haemochromatosis. The pigmentation of bronzed diabetes may, therefore, be regarded as identical with that of haemochromatosis.

It cannot be doubted that the large quantity of iron-containing pigment present in the tissues is derived from the haemoglobin of the blood set free by the disintegration of the red blood-corpuscles. Several cases of haemochromatosis associated with purpura have been reported, while others have presented local haemorrhagic conditions, for example, haemorrhagic pleurisy or pachymeningitis, indicating perhaps some pathological condition of the blood. Nevertheless, in a considerable proportion of the cases observed, including that just described, there has been no evident blood-destruction.

In the cases of bronzed diabetes there two factors present—one, the diabetes with glycosuria, and the other the hypertrophic cirrhosis of the liver. In ordinary cases of diabetes there is no tendency to the deposition of an iron-containing pigment, and there is no evidence that in diabetes there is a marked blood-destruction. The liver suggests itself as a possible origin of the iron-containing pigment, but if the pigment is formed in the liver, it must be carried to the other organs in the form of emboli, and there is no evidence of the occurrence of such emboli nor is there any evidence of phagocytic cells carrying pigment to other organs. The deposition of pigment in the various organs, the heart and pancreas, for example, takes place by just the same method as it does in the liver, so that it seems more reasonable to suppose that the pigment is formed in the cells in which it is found, rather than that it is formed in the liver or other organs and carried to more distant parts.

In association with the accumulation of pigment in the liver there is often cell-degeneration and cell-death, and accompanying this cell-death there is an increase of connective tissue. It seems plausible to believe that the cirrhosis and the inflammation of the pancreas are a result of the death of the cell following the deposition of pigment.

In all cases of bronzed diabetes which have been described there has been found a chronic inflammation of the pancreas. The fact that the chronic interstitial pancreatitis is an etiological factor in the production of diabetes has been pointed out by many observers. The diabetes in these cases seems to be a result of the chronic inflammation of the pancreas and to be a terminal event in the haemochromatosis. The original factor, then, would be some blood-destroying cause, which in many cases is very obscure. Following this blood-destruction there is a formation of iron-containing pigment, which is deposited in various portions of the body; with this deposition of iron pigment there is a cell-death, and a consequent interstitial inflammation of certain organs, particularly of the liver and pancreas. When the pancreatitis has reached a certain degree of intensity, it seems possible to believe that there is an onset of diabetes, thus accounting for the diabetic condition in the bronzed diabetes described by some of the French writers. In the foregoing case the patient's death was caused

by typhoid fever before the pancreatitis had reached a sufficient intensity to cause diabetes.

Discussion.

Dr. Welch:—This is the first instance I have seen of this condition, and about all I know of it is from a study of Dr. Opie's specimens. It has interested me very much indeed and he has said I think practically everything that can be said as to the interpretation of the condition.

I should judge from what I have read of the literature that it is impossible to explain the condition as the result of the formation of pigment from haemorrhages and equally impossible to explain the pigment as being formed in one organ and transported to other parts of the body. Dr. Opie has made very clear the objections to either of those explanations and also the conception of the condition as a disease by itself—a haemochromatosis with change in the liver, pancreas and elsewhere as secondary symptoms. It hardly seems easy to understand how mere destruction of red blood-corpuscles which occurs in many conditions can be an adequate explanation. We have in other conditions, as in pernicious anaemia, extreme destruction of corpuscles and a deposit of pigment, but not like this. The chemistry of the process must be somewhat different from ordinary destruction of the blood. Otherwise how can we account for the fact that this is a definite and peculiar disease whereas the mere destruction of the red corpuscles, following definite lines, does not produce the condition? May not the destruction of the corpuscles, although we can not define the character of it, be a peculiar kind of destruction?

Dr. Osler:—The condition has interested me much in connection with the question of cutaneous pigmentations apart from Addison's disease. We have had a very interesting series of cases within the past few years, two in connection with hypertrophic cirrhosis. One case, a young man upon whom Dr. Halsted operated under the supposition that he might have a tumor in the liver, proved to have a hypertrophic cirrhosis with an extreme degree of pigmentation of the skin. A fourth case of hypertrophic cirrhosis has recently died in West Virginia and specimens of the liver were sent to me and I would ask Dr. Opie to examine them. This case also presented an extreme degree of pigmentation. Two of our cases of enlarged spleen have had considerable degrees of staining of the skin. Occasionally in pernicious anaemia you meet with a degree of pigmentation that looks like Addison's disease and you are in doubt as to the nature of the case. Finally, you have certain instances in which you can not account in any way for the profuse pigmentation of the skin as is the case with the man present now in the ward. He has chronic pericarditis and has not the three cardinal symptoms of Addison's disease.

It seems to me a little doubtful, considering the variety of conditions, in which widespread pigmentation can occur, whether we should accept the view that it is a separate and distinct disease, particularly when we know that pigmentation does occur so often with cirrhosis.

Dr. Opie:—It may be said in answer to Dr. Welch's question that there seems to be some condition necessary to the production of the cirrhosis and pigmentation in addition to the mere destruction of red blood-corpuscles. There have been various attempts to reproduce the pigmentation of haemochromatosis by the injection of substances which cause breaking down of the red corpuscles. Toluylenediamin has been injected subcutaneously into dogs and the organs studied later. In such cases a pigment having the characteristics of haemosiderin is formed in the liver but it is present in moderate degree and cirrhosis is not produced. Attempts to reproduce a condition of general pigmentation by such methods have failed. Recently Kretz has studied a series of cases of cirrhosis of the liver and in about one half of them has found the deposition of an iron-containing pigment in large quantities in the liver. He comes to the conclusion that with certain varieties of toxaemia there is a destruction of the liver cells producing cirrhosis and at the same time this poison, whatever it may be, circulating in the blood, causes a destruction of the red corpuscles. In this combination of blood-destruction and injury to liver cells he finds a favorable condition for the deposition of an iron-containing pigment. This is for the most part theoretical.

Report of a Case of Combined Typhoid and Quartan Malarial Fevers. Dr. Craig.

In the absence of Dr. Craig, Dr. Thayer presented a report of the following case, which occurred at the Sternberg U. S. A. General Hospital at Chickamauga Park.

Dr. P. had suffered from September 29 to October 5, from general malaise, constipation and headache, with an even temperature from 101°F. to 102°F. Although feeling ill, he did not take to his bed until October 5, 1898, when he was admitted to the hospital, complaining of a severe headache and great nervousness. The previous evening he had had a slight chill. On admission, he presented the following clinical symptoms: Gurgling, and much tenderness in the right iliac fossa, a dry, hot skin, brilliant eyes, with injected conjunctivae, and a typical typhoid tongue. The typhoid symptoms gradually increased and he had tympanites, epistaxis, rose-spots, extreme restlessness and a slight bronchitis.

October 12, or about the twelfth day of the fever, his blood was tested by Widal's test and gave a very pronounced reaction, while the urine showed the diazo-reaction very markedly. The patient had never suffered from typhoid fever previously.

Until October 15 the patient continued to present the characteristic picture of typhoid fever, his temperature ranging between 101°F. and 104°F. Baths were given, but they reduced the temperature only a little, and the patient's condition was grave. On October 15, the temperature in the morning had fallen to 100°F., the patient's general condition being very much improved, when he had a slight chill, with a rise of temperature to 103.4°F. The attending physician thought little of the chill, as by evening the temperature had fallen to 101°F., and for the succeeding two days ranged between 100°F. and 102°F. October 18, however, just 72 hours after the first chill, a second and more severe chill occurred, the temperature rising to 104°F. At this time I was called upon to examine the blood, and found the quartan

malarial organism in abundance. The details of this examination will be given later. The patient's general condition was markedly altered for the worse, he being very weak and tremulous, having great general pain and a poor irregular pulse.

From October 18 to October 21 his temperature ranged between 98.8°F. to 100.6°F. The administration of quinin in small doses (5 grains night and morning), was begun October 18. October 21, a third paroxysm occurred, but was delayed somewhat, (probably by the quinin), so that it extended into the 22nd, the acme of the fever being reached by 4 a. m. of that day. This paroxysm was very severe, the chill lasting 30 minutes, and the temperature rising from 99.2°F. to 104.6°F. A fourth paroxysm occurred October 25. For some reason the quinin had been stopped upon the 23rd. A fifth paroxysm occurred October 28, after which time quinin in large doses (10 grains every 4 hours) was given. October 31, a very slight chill occurred, with a rise of temperature to only 102°F.

From this time the patient had no further paroxysms, and his temperature remained normal. The convalescence was very slow. During the malarial complication the patient's condition was that of a desperately sick man, and none of the surgeons who saw him entertained any hope of his recovery. He became extremely emaciated and anemic, and was delirious much of the time. During the whole time, his blood showed numbers of quartan plasmodia, corresponding in their development with the time of the paroxysms. The blood also gave a pronounced Widal reaction whenever tested.

Microscopical examination of the blood.—The blood was first examined at the time of the second chill, when numerous full-grown and segmenting quartan organisms were found. Examinations were made every day, and plasmodia were always easily found. The last plasmodium seen in the blood was on November 31, a full grown quartan organism.

A record of four days, which follows, shows the average findings for that period throughout the course of the fever:

October 18, chill. Large number of full-grown organisms, a few segmenting bodies, fragmenting bodies, and extracellular bodies, and a few hyalin bodies.

October 19. Numerous hyalin, unpigmented bodies, small pigmented bodies, and one fragmentation form.

October 20. Many half-grown and nearly three-quarter grown pigmented quartan organisms, a few vacuolated.

October 21, chill. Many full-grown organisms, several segmenting bodies, and fragmentation and extracellular forms.

Study of the type or organism.—The smallest forms resemble the tertian hyalin form exactly, being amoeboid, though rather less so than in the tertian variety, and occupying generally one or the other side of the corpuscle. As they grew, however, the outlines became more clearly cut than that of the tertian, their movements were slower and their protoplasm presented a very refractive appearance and looked as though it might be finely granular. At this time the pigment began to appear as very dark, rather coarse dots and grains, which were very sluggishly or not at all motile. The shape of the organism at this stage altered very little and very slowly. The red corpuscles containing the organisms were noticeably smaller than the uninfected ones, and were generally of a dark-greenish color. When full-grown, (about 68 to 72 hours old), the organisms had clearly cut outlines, were oval or round in shape, and occupied about two-thirds of the infected corpuscle. The pigment was collected at the edge of the organisms, was almost immobile and dark and coarse. The segmenting bodies, which were always present at the time of the paroxysm, were very characteristic. The segments numbered from 6 to 12, the pigment was collected in the center in one solid, dark block, or in a radiate manner, and nearly all were beautifully regular in their arrangement. Degenerate forms were often observed, in which fragmentation and vacuolization had taken place. No flagellate forms were observed. Peculiar oval extracellular forms were noticed, in which the pigment was motionless. There can be no doubt that the organisms belonged to the quartan type, and there never was a time during the active course of the fever that these organisms could not be demonstrated in the blood, although they disappeared rapidly after quinin in sufficient dose had been administered.

Up to October 15, the twenty-second day of the disease, the course of the fever had been typically typhoid and the temperature curve had begun to decline gradually, as is characteristic of that disease. On the 22nd, following the chill, the temperature rose, but instead of falling to normal or below fell only to the point held previously by the original disease. From that time a gradual decline took place until the second chill, on the 18th, when the temperature rose from 99.4°F. to 104°F., but fell in the course of 4 hours to 99°F. If we leave out the rise of temperature due to malaria, the course of the temperature is that of a typically declining typhoid, which holds true up to the 24th, when the temperature between the malarial paroxysms became very irregular. Prior to the 24th the temperature curve illustrated most instructively how these two diseases, which existed together, influenced the temperature chart.

In the latter part of November, when the Sternberg Hospital was closed, the patient was transferred to another hospital, where he died.

Discussion.

Dr. Osler:—I believe this is the first instance in which the quartan infection has been demonstrated in connection with typhoid, is it not?

Dr. Thayer:—Yes.

Dr. Osler:—This then completes the history, for the estivo-autumnal and tertian varieties have been repeatedly found. I arise again to enter my protest against the term "typho-malarial" for these infections. We do not speak of dysentero-malarial or pneumo-malarial and we should not speak of typho-malarial. The malaria does not seem to influence the course of the typhoid.

It would be interesting to compare this case with the remarkable case of pseudo-typhoid that is now in the ward. During the whole course of the disease chills have occurred associated with profuse sweats, and I do not suppose any one without careful examination would doubt the diagnosis of malaria in such a case, were it made, though I think the evidence at present is strongly in favor of its being typhoid.

Dr. Thayer:—I think the reports that are gradually coming in from various military hospitals with regard to the fre-

quency of these combined infections are rather interesting. Early in the fall and summer the papers were full of statements that cases of combined malaria and typhoid were very frequent and it was said that ten or fifteen, perhaps even twenty per cent. of all the cases were of the combined type. As the accurate reports are received, it is surprising to me to find how few cases have occurred. The conditions that existed in the army camps, in Cuba and in the South, were the ideal conditions for malaria and typhoid to develop together. One would expect that a very considerable number of cases of combined infection should occur, but as a matter of fact such cases seem to have been relatively few. Dr. Norton noted the fact that many cases of typhoid fever at autopsy showed evidences of preceding malaria, but he did not remember, I think he said, a single instance where they were positively found in the hospital. I think we may say safely that the actual course of typhoid fever is very little influenced by the combined infection with malaria. When the two diseases occur at the same time the condition of things seems to be very much that shown in Dr. Craig's case, the malarial symptoms are simply imposed upon those of typhoid. They may aggravate the disease and make the patient feel worse, but they do not affect the course of the typhoid itself, and we must absolutely abandon the name typho-malarial as suggesting a combination of the two diseases.

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VOLUME TO COMMEMORATE THE 25TH YEAR OF DR. WELCH AS A TEACHER AND INVESTIGATOR.

It is customary in Germany for the pupils of a great teacher to express their appreciation and gratitude by dedicating to him a volume of their contributions to learning. The pupils of Dr. Wm. H. Welch of Baltimore have decided to give expression to their regard for him in a similar way and the publication of a volume to mark his twenty-fifth year as a teacher and investigator is now in progress.

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BULLETIN

OF

THE JOHNS HOPKINS HOSPITAL.

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THE RECOGNITION OF THE POISONOUS SERPENTS OF NORTH AMERICA.*

By Howard A. Kelly, *Professor of Gynecology The Johns Hopkins University and Gynecologist-in-Chief The Johns Hopkins Hospital.*

I have felt an interest in snakes since boyhood, but the more practical duties of life have prevented my following this penchant for over twenty years. It becomes now, however, my pleasure to brush up the forgotten lore in order to put before you certain facts I think you should all master before graduation. If our medical curriculum were not already crowded, I should urge a brief course of lectures year by year, followed by an examination, upon the subject of the various poisonous insects and animals and their antidotes; for to whom shall the victim of injuries sustained in this way appeal for accurate information as to the danger from a given bite or sting and the identification of the species causing it, as well as the proper treatment, if not to you?

I shall speak briefly this evening of one group of poisonous animals—the snakes; and it shall be my effort to impress upon you such details of their structure that you shall be able to decide with certainty whether a given species submitted for your examination is or is not poisonous.

In classifying and identifying the various species you will find somewhat useful, although often confusing, Baird and Girard's Catalogue of North American Reptiles in the Museum of the Smithsonian Institution, Part I, Serpents, published in 1853; Jordan's Manual of the Vertebrates in the Northern United States, 1899, is most valuable, and Leonhard Stejneger's work on the Poisonous Snakes of North America is indispensable; the last-named work published by the government for the Smithsonian Institution really ought to be in the hands of every physician in the land. Dr. Yarrow, of Washington, one of our most eminent authorities, has written numerous treatises, including an article in Wood's Reference Handbook of the Medical Sciences. Other works are a Catalogue of Snakes in the British Museum, in three volumes, by Boulenger, London, 1893; Herpetologia Europæa, by E. Schreiber, Braunschweig, 1875, and Deutschland's Amphibien und Reptilien, by B. Dürigen, Magdeburg, 1897.

Snakes are reptiles distinguished from batrachians (the frog family) by the fact that they undergo no metamorphoses and do not pass through a tadpole stage of existence. Snakes either lay eggs and are oviparous, or they produce their young living from eggs hatched but a short time before inside the mother, when they are ovoviviparous; they are distinguished from the lizards by possessing widely dilatable mandibles and the fact that the head-bones are united by ligaments, while they possess no limbs or shoulder-girdle, and have no eyelids

*An address with a demonstration to the Graduating Class in the Medical School, before the Johns Hopkins Hospital Medical Society, November 6th, 1899.

and no external ear or tympanum. In boas there are little rudimentary hind limbs.

The body of the snake is covered with scales arranged in rows down the back and on the sides; large transverse overlapping scales in a single row cover the belly. The head, as in the lizards, is covered with a series of large plates which are constant in their arrangement in the same species, and therefore important aids in classifying and identifying species.

One might suppose from this statement that nothing would be easier than to determine whether or not a given animal is a snake; there are, however, several little animals which are popularly considered as snakes which belong in other orders. I show you here for example an animal, the Amphiuma means, widely known as the "Congo snake," and looking much like an eel, but able to live a long while out of the water. On close inspection you will discover four short rudimentary limbs with little toes, and on each side of the neck there is a spiracle. In walking the Amphiuma uses these feet, useless as they appear to be, as I have frequently had occasion to observe in this specimen which I kept alive for some time. It is one of the tailed batrachians, and therefore much more closely allied to the frogs than to snakes.

While the Amphiuma comes from a lower order than the snakes and much resembles a fish, I show you here on the other hand a beautiful lively little animal everywhere known as a "glass snake," the Ophisaurus ventralis, belonging to the family of the lizards, which has a long cylindrical snake-like body closely covered by overlapping scales; it is over two feet in length, without any trace of limbs, and necessarily adopts the same mode of progression as snakes. The Ophisaurus is, however, distinguished from the snake, upon closer examination, by solidity of the head, the well-defined ear-openings near the angle of the jaw as well as the distinct eyelids. It has also this distinguishing characteristic: the vent lies about one-third of the length of the animal back of the head instead of nearer the tail. I received this fine specimen from Dr. John C. Rodman, of Wilmington, N. C., who writes me that its captor told him that if struck with a whip it would break into a number of pieces, which if let alone will come together again in the course of an hour.

The Ophisaurus is a gentle and perfectly harmless little creature, and so is the Congo snake, which feeds on worms and crawfish. There is in the whole world no known poisonous member either of the batrachians or of the lizard family, popular superstition to the contrary, with the single exception of these two large lizards which I here show you, the Gila monsters (Heloderma suspectum), received from Dr. John S. Pearce, of Albuquerque, N. M.

They are so sluggish that I have never seen them attempt to bite; the most they have done in the couple of months they have been in my possession has been to crawl slowly around their cage and eat the eggs on which I feed them.

Among the true snakes, the Ophidians, we must distinguish carefully those which are poisonous from those which are not, and not be misled by a widely prevailing notion that all snakes are poisonous and ought therefore to be destroyed. As an example of the misfortune of ignorance on this head, I may cite the experience of a prominent Baltimore doctor who, while fishing in one of the rivers near town and letting his hand hang in the water, was bitten by a harmless water-snake (probably Tropidonotus sipedon), and for fear that he was poisoned he immediately consumed a large amount of whisky to act as an antidote.

No ophiologist I know of takes the ground that poisonous snakes should not be destroyed, but the ignorance which leads people to destroy all snakes alike does not tend, as they think, to promote the extermination of the poisonous species, but in fact actually tends to preserve them, as their worst enemies are some of their own congeners of the harmless species, such as the black and the king-snakes (see Fig. 1).

The ignorant prejudice which leads people to destroy snakes indiscriminately tends further to seriously disturb the balance of nature by favoring the increase of the small animals upon which they naturally feed, such as toads and frogs and particularly the destructive field-mice which are consumed by thousands.

With a view, therefore, of giving you this information, which may at any time become a matter of vital importance to your patients, as well as with an earnest desire to save the innocent species, I shall now point out to you certain differential points between the poisonous and non-poisonous forms by which they may be most readily distinguished.

Fortunately the poisonous species are few in number and readily distinguished after one has once carefully noted some of their characteristic marks.

The poisonous snakes of this country, with the single exception of the little harlequin-snake (Elaps) of Florida and the South, belong to the group known as "pit-vipers," that is to say, they possess a curious conspicuous blind depression, which is a prominent anatomical characteristic in the fore part of the head over the upper lip between the eye and the nostril in what is known as the loral region. This pit is hollowed out in the thick short superior maxillary bone, which here has the sole function of supporting the poison-fangs. Zoölogists have never been able to determine the function of the pit; Professor Leydig, finding it supplied with a large nerve not unlike the nerve of the eye and of the ear, has concluded that it is the organ of a sixth sense. The pit-vipers differ from the harmless snakes further in that their heads are triangular, with massive maxillary development expressive of great muscular power in the jaw; they have fewer large scales on the head, and a greatly increased number of small scales taking their place, giving the head more of a warty appearance. The snake is thicker in proportion to its length and has a shorter tail, and the dorsal scales are keeled, making the surface conspicuously rough. The pupil is elliptical. If the mouth is opened, the usual number of small teeth are seen in the lower jaw, while, above, a row of recurved short teeth is seen well in towards the centre of the head; these are the palatal teeth, while just outside of these, under the lip and well toward the front are two long mucous folds which hang like veils over the powerful recurved fangs which lie concealed with a number of smaller reserve fangs behind them. If the snake is living, as in the case of the copperhead which I now show you, he is apt upon touching the fangs to throw one or both forward, projecting and erecting them as in striking; further if the edge of a saucer or a watch-glass such as I hold

here is placed under the fang, a convulsive movement may be started by which the animal endeavors to thrust his fangs into the object and then rotates the maxillary bone inwards so as to bring them violently towards the gullet with the ejection of a few drops of the clear yellow poison. In a large diamond-back rattler a teaspoonful of poison may be ejected. For a description of the mechanism see S. Weir Mitchell's report to the Smithsonian Institution.

The poison-fangs are shed from time to time; I show you one dropped a few days ago in my library by this large banded rattlesnake, which is also just about to shed the opposite fang, which I now remove.

I will now characterize the pit-vipers a little more closely by stating that there are three genera with somewhere about 18 species, and all but two of these belong to the rattlesnakes, which are easily recognized by the caudal appendage.

The genera are Agkistrodon, Sistrurus and Crotalus.

The two snakes to which I now call your attention are the copperhead and the water-moccasin, both belonging to the same genus, Agkistrodon, and known respectively as Agkistrodon contortrix and Agkistrodon piscivorus.

The distribution of the copperhead (Agkistrodon contortrix), says Stejneger, "in a general way is coëxtensive with that of the banded rattlesnake (Crotalus horridus), though as a rule it does not extend quite so far north. As a compensation it goes considerably farther south in the western portion of its range, extending into the southern part of Texas."

I exhibit here two well-developed adult copperheads, received from Dr. Rodman, of Va., and Dr. Goss, of Georgia. The color as you see is a light chocolate, with wave-like dark alternating patches on the sides, the belly is yellowish; there are twenty-three rows of scales from side to side, all strongly carinated. The copperhead I think the handsomest of all our snakes. The arrangement of the scales on the head can be seen in the drawing made by Mr. Becker; the particular point of difference here between the copperhead and the moccasin lies in the presence of the loral plate in the copperhead, and its absence in the moccasin (see Figs. 2 and 3).

Although vicious and usually striking without warning, the copperhead is not so dangerous as the rattlesnake when the poison is taken volume for volume; its bite is also less liable to prove fatal, as the snake rarely exceeds three feet in length, and the amount of poison available at any given time is much less than in the larger rattlesnakes.

The moccasin (Agkistrodon piscivorus) is distinctively a water-snake, and is of dark greenish brown color, sometimes almost black, variegated by a series of darker but indistinct bars. The twenty-five rows of dorsal scales are carinated. The lower wall of the eye is bordered by the third labial plate, counting back from the rostral in the middle of the upper jaw (see Figs. 4 and 5). The loral plate is absent. The moccasin, or cottonmouth, as it is often called, can easily be distinguished from other snakes by the following marks: In the first place, its general configuration broad in proportion to length, the triangular head, the thick jaw, suggest at once that it belongs to the vipers; a closer examination shows that it possesses the characteristic pits between the eyes and the nostrils, settling the fact that it is a pit-viper. It then only remains to distinguish it from the group of rattlesnakes on the one hand, which is easily done by the absence of the characteristic caudal appendage; and on the other hand from the copperhead, its closest ally, and this is easily done by the remarkable difference in color, the copperhead being of a lustrous copper-color, while the markings of the water-moccasin are all more or less obscure, and it possesses no beauty of coloration.

A further distinguishing and characteristic mark is a narrow yellowish white line beginning below the eye and passing backward and crossing the angle of the mouth at the seventh labial, as shown in Mr. Becker's drawing.

Although there is everywhere felt a wholesome dread of the moccasin, and Jordan calls it "the most dangerous of our snakes," I know of but one recorded fatality. Dr. J. R. Hopkins, of Hopkins, S. C., tells me that the cattle in his country are sometimes bitten when drinking in the branches and return with their heads much swollen.

I will be brief in considering the rattlesnakes, so easily recognized by their specific appendage, the rattle at the end of the tail. There are two genera, Sistrurus and Crotalus; Sistrurus, at the time I last took an active interest in snakes, was known as the little rattlesnake, or the prairie-rattler, belonging to the genus Crotalophorus or Caudisona. The two species, inhabiting the United States, recognized by Stejneger, are the massasauga (Sistrurus catenatus), and the ground-rattlesnake described by Linnaeus (Sistrurus miliarius). Although there is a popular dread of these animals, there is reason to question whether their bite is ever fatal.

In the form of the head and its broad plates, the snakes of this genus are more nearly allied to the harmless Colubers than any of the Crotalids.

I have here three living rattlesnakes representing two species: the first two are specimens of Crotalus horridus, the banded rattlesnake; one of these, so black as to scarcely show any markings, comes from central Pennsylvania, while the larger snake, 50 inches in length and 7¼ in circumference, is a beautiful specimen from Dr. Goss, in Georgia; he has buff, finely mottled background, crossed at frequent intervals by rich velvety zigzag lines from two to three scales in breadth. In order to emphasize the remarkable contrast between these poisonous vipers and some of the harmless snakes, which I shall produce presently, note that of the entire 50 inches but 4 inches is tail. All the rattles of this larger snake have been lost, so that when he vibrates his tail as now there is no sound whatever unless the end of the tail strikes a hard or dry surface; this disposes of the common notion that the number of rattles is any indication of the age of the animal; note also, as I open the mouth, that the fang of one side has been shed, and the other is just ready to drop into the watch-glass which I hold under it.*

The curious pit, so distinctive of our vipers, is well defined and measures 5 millimeters in depth.

I also show you here another beautiful Crotalus, received from Oklahoma, through Mrs. J. W. Putts of this city, 43½

* Two large new fangs were found in position, ready for service, two weeks later.

inches long, powerfully built in proportion to his length, with six rattles which are vigorously agitated at the slightest provocation. I have had some difficulty in identifying the species. Dr. Stejneger, of Washington, however, decides that it is the prairie-rattlesnake (Crotalus confluentus), which, in some specimens, shows more green The ground color, in remarkable resemblance to the sage-bush of the prairies, is of a yellowish green broken by a series of dorsal oblong blotches which are more or less quadrangular in form, edged by a lighter streak. On the sides between the blotches and belly-scales there are two rows of dark spots, which coalesce in the tail region with the blotches so as to form half rings; the head has the characteristic form, is markedly triangular, with powerful jaws, and looked at from above it is covered with tuberculate and carinated scales; (see Fig. 6) the only large scales seen are the strongly developed superciliaries which project far over the eye, each of which is traversed by a fine yellow line bifurcating at its median end; looked at from the side the head-scales are all larger and there are two striking yellowish streaks extending from the angles of the eye back to the angle of the mouth. The large rostal scale is marked by a white line on the margins.

The harmless snakes, the Colubers, are much more abundant than the poisonous varieties just mentioned and can easily be distinguished from them even upon a superficial examination of their slender form, the large scales covering the head, the smooth scales covering the body in many species, together with the absence of the maxillary pit. When the mouth is opened two long rows of small teeth are found in the upper jaw attached to the palatal and the maxillary bones. The numerous small curved maxillary teeth on the long maxilla replace the single large fang on the short quadrate bone found in the vipers. Many people are afraid of handling the Colubers, dreading the bite and an extensive lacerated wound. The fact is that the bite of the largest of them, 5 or 6 feet long is quite insignificant. I have myself twice been bitten recently by a large blacksnake and by this large, powerful water-snake; a few trifling punctures and a few drops of blood were the only result, and the wound healed as though the skin had been pricked by a needle. Any one of these snakes will attempt to make his escape when encountered, but most of them will fight when cornered, or when picked up for the first time. The blacksnake particularly deserves his reputation as a fighter; one which I have been keeping in the country in a large vivarium is always ready to fight me every time I enter.

As an example of a fine Coluber here is a corn-snake (Callopeltis guttatus) looking much like a blacksnake, 55 inches long, with 27 rows of scales across the back, and on close inspection those towards the middle are found to be faintly keeled while the lateral ones are smooth. The usual coloration of this snake is a reddish-brown color with a row of blotches down the back. In this specimen the color is almost uniformly a dull reddish black. Closely allied to this is the pilot-snake, which is one of our largest serpents, measuring six feet or more.

Here is another beautiful, graceful, harmless snake, one of the slenderest of our large snakes, known as the coachwhip (Masticophis flagelliformis), received from Dr. Goss in Georgia. This specimen is 79¾ inches in length. The fore part of the body, as you observe, is jet black above and below, and shades gradually backward into a dull white; the tail is particularly beautiful, as the smooth scales there become broader and margined with a darker streak marking each wart and giving it a tesselated appearance. The eye of this snake is large and handsome, while the pupil is surrounded by a reddish iris which gives it, under the overhanging superciliary, a particularly striking lustrous appearance, not unlike the imitation snakes made in the form of bracelets by the jewelers. I show here the arrangement of the scales of the head, giving the peculiar elongate vertical plate with the large superciliaries and occipitals. Note that although the length of the jaw as measured to the commissure is only 33 mm., the real length is 40 mm., as the angle of the jaw lies well behind the commissure, showing that the capacity to swallow is much greater. than would at first sight seem possible.

I shall not pause to dwell on the specific characters of a number of snakes I here show you which are manifestly harmless; among them are the young of the hognose viper (Heterodon simus), the exquisite slender little green snake (Opheodrys aestivus) from Georgia, and a little Storeria Dekayi of a dim or slate color, with small dark spots on the back, only ten inches in length and three-sixteenths of an inch in diameter.

Most important is it that you should learn to recognize and differentiate certain perfectly harmless snakes which through ignorance have acquired a bad reputation. Here, for example, is a full-grown hognosed viper, or spreading, puffing or blowing adder (Heterodon) as it is often called, one of our most valuable serpents in the destruction of field-vermin, found over a wide geographical range, and everywhere in ill-repute as deadly poisonous, and yet perfectly harmless and most gentle and easily tamed. When first alarmed this snake flattens himself out until the upper part of his body and his head are spread out like a thin skin and bearing a remarkable resemblance to the hood of a cobra. He then draws in wind and forces it out with a loud hissing sound, presenting on the whole a most threatening and forbidding aspect. Even if you were to pick him up and he bit you, the bite would not amount literally to more than the pricking of "a row of pins."

Of this "viper" there are two species, one blackish and the other with considerable yellow or reddish in the background, respectively Heterodon niger and Heterodon simus, both of which are easily distinguished by the "hognose," or retroussée nose, formed by the projecting turned-up rostral scale. (See Mr. Becker's drawing, Figs. 7 and 8.)

Another snake with a bad reputation is this one, which came to me from Alabama, labeled "orange-bellied moccasin," "deadly poisonous," which is really only a large water-snake (Tropidonotus, or Natrix) found abundantly everywhere and not resembling in the least any form of poisonous serpent except in his natural vicious, ugly disposition. He is confused with the true moccasin (Agkistrodon) because he is dull in color and found about the water in the same localities, and is rough-backed with prominent carinated scales; but a glance at the head, which is elongate and colubriform, the

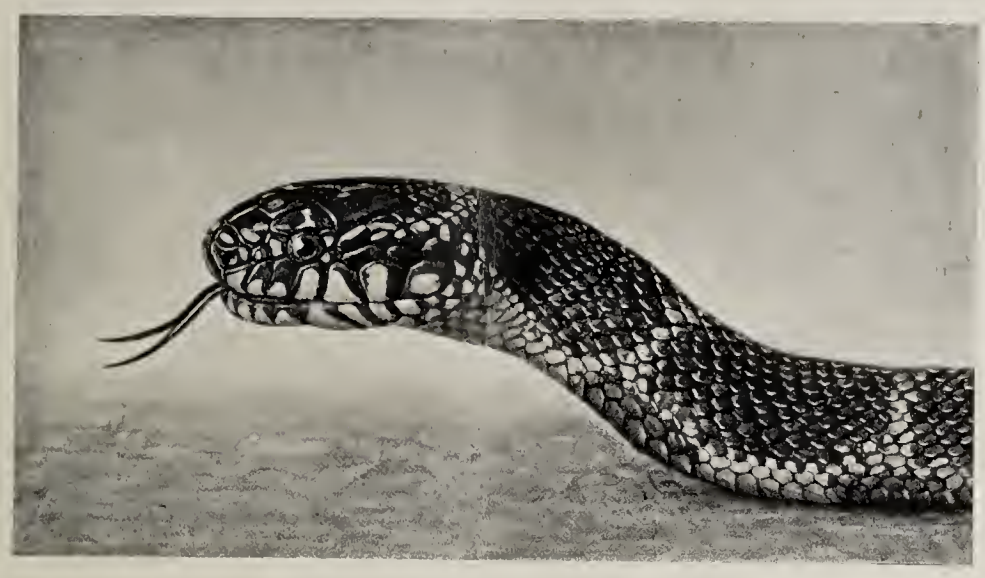


FIG. 1

Ophibolus getulus, king snake, or chain snake, one of the most beautiful of our harmless snakes, found through the South and as far north as Maryland, invaluable in the destruction of vermin. The markings are black and white or yellowish. The loral scale is seen between the anteorbital and the nasal. The absence of a pit and the form of the head show that this is not a poisonous snake.



FIG. 2

Agkistrodon Contortrix, Copperhead, a common pit viper of wide distribution, belonging to the same genus as the moccasin. The most marked difference in the scutellation of the head lies in the presence of the loral scale, between anteorbital and nasal in the copperhead, and its absence in the moccasin.



FIG. 3



FIG. 4.

Agkistrodon piscivorus, true moccasin. The head is large and triangular with massive jaws. The plates and scales are large. The pit is well shown on a line joining the nostril with the lower border of the eye. There is no loral scale between the nasal and the anteorbitals. The markings on the side of the head are characteristic. Those on the body seen in Fig. 4 are often obscure.



FIG. 5.

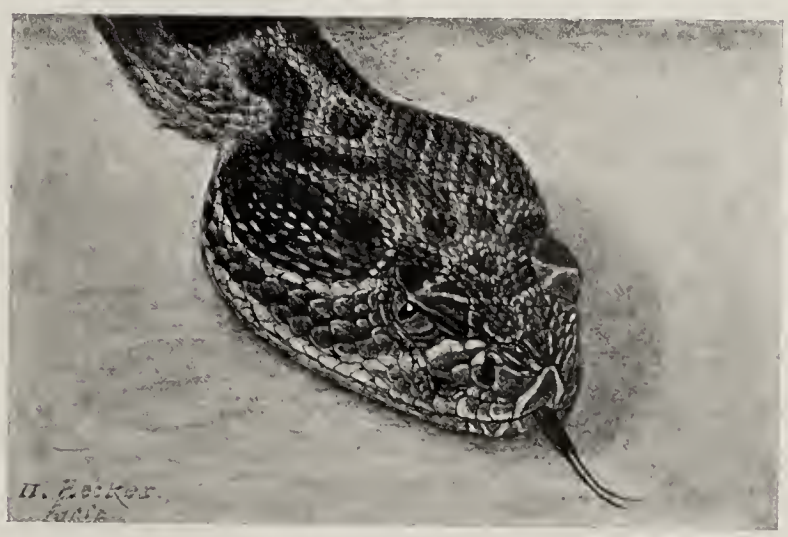


FIG. 6.

Crotalus confluentus, "Prairie rattlesnake," from Oklahoma, one of the group of rattlesnakes with square blotches on the back.

Note the absence of large scales on top of the head, with the exception of the projecting superciliaries. The pit is seen below and behind the nostril. The arrangement of the lines on the head is characteristic of the species.



FIG. 7

Heterodon, puffing adder, hognosed viper. A harmless and valuable but threatening looking snake. The turned-up rostral plate at the end of the snout is the characteristic mark of the genus.



FIG. 8

This snake has the power of flattening out its head and the upper part of the neck until it bears a remarkable resemblance to a cobra.



FIG. 9

Natrix Sipedon, water snake, often erroneously called "water moccasin," and confused with the true moccasin (agkistrodon), a pugnacious but a harmless animal. The head



FIG. 10

is narrow, oval, and the vertical plate between the eyes is also narrowed in remarkable contrast with the true moccasin (see Fig. 4). There is no pit.

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absence of the pit and the side-lines so characteristic of the true moccasin at once serve to differentiate the two. (Figs. 9 & 10.)

The Tropidonotus is a snake not so useful as our land-snake, as he lives on fishes and frogs, and I am willing to admit the question whether he ought not to be killed.

"Highland moccasin" is another term applied to a harmless snake which on account of the unfortunate name is condemned to be killed wherever he is found.

I trust that this demonstration with the living forms before you will impress upon you the easily recognized differences between poisonous and non-poisonous forms so that you will feel yourselves not only equipped to decide in case of accident whether the bite of a particular snake is liable to be followed by dangerous symptoms, but that you will constitute yourselves as well defenders of the harmless snakes, which are not only of great economical value but aid as well in the destruction of the poisonous forms.

ON THE CHEMISTRY, TOXICOLOGY AND THERAPY OF SNAKE POISONING.*

By Thomas R. Brown, M. D.

In this portion of the country, the subject of the poison of venomous snakes and the treatment of snake-bite is rarely brought to our notice, due of course largely to the extreme rarity of the condition and the paucity of snakes of high degrees of toxicity.

Nevertheless, when one considers that in India alone the lives of more than twenty thousand human beings and sixty thousand cattle are annually sacrificed to the poisonous Ophidia, and that in Africa, Australia, Central and South America and the islands of the Indian and Eastern Pacific oceans many deaths occur annually from the same cause, it will be seen that the subject is one of sufficient magnitude to appeal to every one interested in the general subject of medicine in its broader sense.

Indeed, we have but to turn the pages of the journals devoted to bacteriology, chemistry and toxicology for the past ten years to recognize how much work is being done in this direction and how marked are the advances recently made in our knowledge of the subject.

Before going more carefully into the chemical and therapeutical side of the subject, it will be of interest to sketch briefly the morphological and zoological characteristics of the poisonous snakes and to mention the most important representatives and their geographical distribution.

The great family of snakes—the order Ophidia, has three divisions, the O. colubriformia which are innocent, the O. colubriformia venenosa and the O. viperiformia, the last two of which are poisonous and compose the Thanatophidia—a well merited name when one considers their great destructiveness.

A rapid and easy method of differentiating the innocent from the poisonous snakes is by an examination of their jaws, the harmless snake having two complete rows of small ungrooved teeth, an inner palatine and an outer maxillary, while in the venomous snakes the outer row is represented by one or more large tubular fangs firmly ankylosed to the maxillary bone.

This bone, by its movements, causes the erection or reclination of the fangs.

The maxillary bone is much smaller in the poisonous colubrine than in the innocent snake, while in the viperine snake it is reduced to a mere wedge, giving insertion to a long curved tubular fang. These fangs, when reclined, are covered by a sheath of mucous membrane, in which lie also several reserve fangs in different stages of growth, which are designed to replace the working fang, if it should be shed or lost through accident. The fangs, although described as being perforated, are in reality not so, this effect being produced by a folding of the dense, compact tooth on itself, forming either an open groove as in Hydrophidae, a complete canal as in Cobra or a still more complete tube as in Viperidae.

The poison is secreted by a conglobate racemose gland, almond-sized in the cobra, and opening by a duct into the capsule of mucous membrane, enveloping the base of the fang, the venom thence flowing into the dental canal, the same muscles which close the jaw also compressing the poison-gland and forcing the poison through the duct. At the orifice of the duct, a sphincteral arrangement of muscle fibres has been described by Fayrer in the cobra and by Weir Mitchell in the rattlesnake.

With the exception of New Zealand and the Oceanic Islands, venomous snakes are found almost all over the tropical and temperate regions of the world.

Among the more important of the poisonous snakes we have: in North America, Ancistrodon contortrix (copperhead), Ancistrodon piscivorus (water-moccasin), the many varieties of Crotalus (rattlesnake); in South America, Elaps corallinus (coral-snake), Elaps lemniscatus, Lachesis mutus and rhombata (bushmaster); in Central America, Bothrops lanceolatus (lance-snake); in the West Indies, Craspedocephalus; in Europe, Pelias or Vipera berus (adder), which is found throughout most of Europe, while in Dalmatia, Hungary and Greece we also have Vipera Redii, and in southern Europe, Vipera ammodytes (sand-viper); in Africa, Naja haje (asp), Naja haemachates, Naja noir and Cerastes, while in Australia we have Hoplocephalus curtus (tiger-snake), Pseudechis (blacksnake) and Acanthophis (deaf-adder).

Our knowledge of the Thanatophidia of India is very complete, due to the monumental work of Sir Joseph Fayrer, and it is upon the poison of these snakes that much of the best recent work has been done.

The venomous colubrine snakes of India are: of Elapidae, Naja tripudians (cobra), Ophisphagus elaps (hamadryad), Bungarus ceruleus (krait), Bungarus fasciatus (san kni); of

*Read before the Johns Hopkins Hospital Medical Society, Nov. 6th, 1899.

Xenurelaps, X. bungaroides and the varions species of Callophis; and Hydrophidae, a very numerous and extremely poisonous family of sea-snakes, but, on account of their habitat, not very harmful.

The Indian viperine snakes are represented by: Daboia Russellii (chain-viper), Echis carinata (kuppur, or phoorsa-snake)—these are trne vipers, while the Crotalidae or pit-vipers are only feebly represented by Trimerisuri, Peltopelor, Halys and Hypnale, which are much less poisonous than their American congeners, Crotalus, Lachesis and Craspedocephalus.

In India in 1898, 21,901 human beings died from the effect of snake-bite, and in this enormous mortality, the snakes stood in point of destructiveness in the following order: Cobra, Krait, Echis, Daboia. The toxicity of the venom, besides varying according to the species, varies markedly in the same species and variety.

Thus, the bite of the snakes of the tropics is far more dangerous than of the corresponding varieties in Europe. There is also a marked difference according to the time of year, the bite being more dangerons in the warmer season; in fact, the intensity of the venom in the same snake varies from day to day, being more on hotter days, less on cooler days; also the bites of hungry snakes are less severe than those of well-fed ones.

The poison acts most readily upon warm blooded animals, especially if directed at once into the veins, but it is deadly to cold-blooded animals as well and to the lowest forms of invertebrate life.

Strange to say, a snake cannot poison itself or any of its species, and only slightly any other genus of poisonous snake, bnt innocent snakes it poisons quickly.

In some cases, especially when the victim is weak, or the poison is injected directly into the veins, death is almost instantaneous, while in other cases, death may not occur for a long while, and this may be due to a secondary infection, due to the destruction of the bactericidal properties of the blood by the venom.

As to the locality of the bite, in the great majority of cases this is on the extremities (in 61 of 65 fatal cases tabulated by Fayrer).

According to Fayrer's statistics obtained from his study of 65 fatal cases in India, 7 died under 1 hour, 8 between 1 and 2 hours after the bite, 9 between 2 and 3 hours, and 13 over 24 hours.

The symptoms of snake-bite are both local and general, these differing in relative intensity, according to the conditions of the case and the variety of snake.

Ceteris paribus, the local symptoms are the more marked, the more prolonged the case; while in cases of rapidly fatal termination, they may be practically wanting altogether.

These local symptoms differ somewhat with the variety of the snake, but, speaking generally, consist of a rapidly appearing, inflammatory, local oedema of the affected spot, followed later by more or less ecchymosis and gangrene, with or without pain, and often with the appearance of lymphangitis and local phlegmons. In the Crotalidae, where the local lesion is especially severe, besides the oedema we have extensive gangrene of the affected portion of the body; according to Fayrer, Naja (a colnbrine) kills without destroying the blood's coagulability, while Daboia (a viperine) produces complete permanent fluidity.

The constitutional symptoms are to be ascribed to a poisoning of the cerebral and spinal centres, especially those of the mednlla, inducing general paralysis, especially of respiration, paresthesias, and precordial pain.

Besides these we often have a marked tendency to hemorrhage from the various organs of the body (hematuria, hematemesis, etc.), diarrhea, vomiting, disturbances of vision and amaurosis, headache, dizziness and violent dyspnoea.

In cobra poisoning we have an especially rapid destruction of the respiratory functions, but the pupil of the eye is not affected, while in daboia poisoning, we have wide pupillary dilatation; there is also a greater tendency to convulsions in cobra poisoning. The cause of death may be (1), general paralysis, especially paralysis of respiration, (2), tetanic arrest of cardiac action, probably due to the action of the venom upon the cardiac ganglia, (3), a combination of these causes, (4), secondary infections of varions characters, due to the destruction by the venom of the bactericidal power of the serum.

Even in the patients that recover, local paralyses in the most diverse parts of the body may persist for a long time, together with various local manifestations in the portion of the body bitten, paresthesias of various kinds, pemphigoid eruptions and pain.

Of late years, a great deal of investigation has been carried on upon the action of snake-poison, by means of animal experimentation.

Ewing has shown that the normal germicidal power of the serum is entirely lost after poisoning with Crotalus venom, and the same results have been obtained after poisoning by Pseudechis in Australia.

Many observers have shown the marked hemolytic action of the majority of snake-venoms, while Halford and Martin have called attention to the marked increase of leucocytes in the blood of animals that have recovered from snake-bite.

Brunton and Fayrer concluded from their experiments on certain of the mammals and on frogs, that cobra poison, besides paralyzing the reflex action of the cord acts upon the nerve-endings in the muscle as curare does, and Ragotzi, who has confirmed these observations, thinks that "failure of respiration is mainly brought about by this paralysis of the nerve-endings in muscle, and that the direct action of cobra-poison on the central nervous system is altogether subsidiary."

Many other interesting points regarding the physiological action of venoms have been observed, and in many cases slightly different effects have been noted, according to the species of snake from which the venom was obtained, a result not at all unexpected when we remember that there are quite marked differences in the symptoms of human beings poisoned by snakes.

As we shall see later on, however, Calmette regards the primary action of all snake-venom as the same in kind, although differing in degree, ascribing the symptoms at variance in the different cases to the presence of various albnminoid substances in the venoms, which have but little to

do with the real cause of death. Following the line of work instigated by Roux and Vaillard, in the case of tetanotoxine, Calmette and Martin, working separately, have worked out the toxic value of some of the venoms, i. e., the number of grammes of an animal (rabbit), which is killed by 1 gramme of poison introduced subcutaneously.

Calmette's results were—

Cobra, ...	4,000,000
Hoplocephalus curtus, . . .	3,450,000
Pseudechis, ...	800,000
Pelias berus, ...	250,000

while Martin placed the toxic power of the Australian venoms somewhat higher, thus:

Hoplocephalus curtus, . . .	4,000,000
Pseudechis, ...	2,000,000

The diagnosis of snake bite is, of course, easily made from the history of the case and the symptoms, and by an examination of the bitten spot.

PROGNOSIS.

As to the prognosis, this varies markedly with the country, the climate, and the species of snake. If one of the Indian snakes, Cobra, Hamadryad, Bungaris or Daboia, has inoculated its full charge of venom into its victim, the result, according to Sir Joseph Fayrer, is invariably fatal.

In America, Weir Mitchell gives a series with a mortality of 25 per cent., and another with one of 12 per cent., while Ellzey gives 15 per cent. as the usual proportion of deaths.

In Australia, it is given as about 7 per cent.

The much lower mortality in the last two countries probably depends partly upon the greater intelligence of their peoples, and their recognition of the absolute necessity for prompt treatment.

THE CHEMISTRY OF SNAKE-VENOM.

The chemistry of snake-venom should be of especial interest to Americans, because the greatest advances in our knowledge of the subject have come from the work of American investigators, especially Weir Mitchell and Reichert.

Fontana in 1781, and Prince Lucien Bonaparte in 1843, made analyses of viper-poison, and concluded that its toxicity was due to an active principle, achidnine or viperine.

Busk, from the analogy between the poison-gland of the snake and the parotid, suggested that the poison might be in some way related to ptyaline.

Weir Mitchell in 1860, found in the poison of Crotalus, (rattlesnake), two albuminoid substances, one coagulated by boiling and comparatively innocuous, the other not coagulated by boiling and poisonous, and he called attention to the "singular likeness between the symptoms of rattlesnake poisoning and those of certain maladies, such as yellow fever," an analogy already noted by S. L. Mitchell, Majendie and Gaspard, who also called attention to its resemblance to poisoning by putrefying substances.

Gautier, of Paris, ascribed the poisonous properties to a ptomaine, but this has been disproved by Mitchell, Reichert and Gibbs.

Fayrer and Brunton in 1873, showed that cobra-poison remained active after coagulation by boiling. The work, however, which has done most to clear up the chemistry of snake-venom is that of Mitchell and Reichert, the preliminary report appearing in 1886, while the full details of the work appeared later in the Smithsonian Institute Reports.

Their experiments were carried on upon the poisons of the copperhead, rattlesnake, water-moccasin and cobra.

The poison is a slightly turbid yellowish fluid, more or less viscous, always acid and having a specific gravity of between 1.050 and 1.065. Whether in the liquid or dry state, venom is soluble in water with a slight turbidity.

Venoms usually contain 25 to 50 per cent. of solids, but may contain as little as 12 per cent., or as much as 67 per cent., as noted by Martin in some of the Australian snakes.

Venoms dry rapidly at 16° to 20° C. in a desiccator, and the dried residue resembles markedly dried egg-albumin in its physical properties.

This dried venom if kept from moisture apparently keeps indefinitely, Weir Mitchell having preserved some Crotalus venom without apparent diminution of toxicity for 22 years.

In glycerine, also, venom seems to keep indefinitely.

The watery solutions of all the venoms studied, with the single exception of Crotalus adamanteus, can be subjected to the temperature of boiling water without the complete destruction of their poisonous properties. In the exception mentioned—the diamond-backed rattlesnake—the toxicity is completely destroyed by a temperature below 80° C.

The work of these two investigators showed that venom consists of at least two, and probably three, proteid like bodies, two soluble in distilled water, and one not.

Of the two that are soluble, one does not coagulate at 100° C., and this may be obtained by boiling venom which throws down or destroys all the other proteids, and then either dialyzing or filtering.

The various reactions of this body—its positive reaction with the xantho-proteic, Adamkiewicz's and Millon's reagents, the fact that it formed no precipitate with carbon dioxide gas, ferric chloride, copper sulphate, and glacial acetic acid, and that it did form a precipitate with mercuric chloride, absolute alcohol, and potassium ferrocyanide in the presence of weak acetic acid—led them to suppose that it was a peptone and to it they gave the name of venom-peptone.

Some of its reactions were atypical, however; as, its forming a precipitate with dilute acetic acid but redissolving in excess of the reagent, its precipitation by sodium chloride, which precipitate was soluble in an excess of glacial acetic acid; these and other considerations led Wolfenden to call attention to it again and to point out that it is probably, more truly speaking, an albumose. The precipitate formed by adding water to venom was found to have the properties of a globulin, especially of paraglobulin, and was called venom-globulin; while the third proteid present, their venom-albumin, had the properties of an albumin and was considered harmless by Mitchell and Reichert. According to their experiments, the globulin acts more on the respiration, circulation and blood, tending to destroy the red blood-corpuscles, prevent coagulation, produce ecchymosis, lower blood-pressure and paralyze respiration, while the peptone (or albumose) acts more on the

tissues tending to cause oedema, putrefaction and sloughing. While most venoms contain (*a*) a proteid coagulable by heat and (*b*) a proteid or proteids not thrown out of solution by this means, it is nevertheless extremely difficult to assign exact positions to these bodies, because of the somewhat arbitrary and rather artificial means of differentiation at present in vogue, and because of the fact that many of the constituents of various venoms give atypical reactions, rendering it impossible to definitely assign them to any especial group, although the great majority of their properties may harmonize completely with those of a special class, the peptones, the proto-albumoses, etc., for example.

Recent work seems to show that cobra-poison and pseudechis-poison contain proto-albumose, while crotalus-venom seems to contain a body more closely related to the deutero-albumoses.

The amount of proteid coagulated by heat differs considerably in different species; thus, it is 24.6 per cent. in Crotalus, 7.8 per cent. in Ancistrodon, and only 1.75 per cent. in Cobra.

The whole question of the exact position of the various constituents of venom in the proteid family must be left in *statu quo* until a more definite and scientific means of differentiation of the various members is possible.

Until then, by some observers, the venoms will be regarded as made up of globulins and peptones, by others as globulins and albumoses, and by still others as albumoses alone.

A few words may be of interest as to the effect of various substances upon snake-venom, especially as it is because of these reactions that many of the therapeutic measures applied to snake-bite have been suggested.

Venoms are rendered inert by those chemical agents that destroy proteids or precipitate them in insoluble form, such as gold chloride, potassium permanganate, nitric acid and nitrate of silver; the same effect is noted with the hypochlorites, and also with more prolonged action of carbolic acid and the caustic alkalies.

Although Mitchell found that the venom of Crotalus was destroyed by gastric digestion, the venoms of Cobra, Pseudechis and Pelias berus have been shown to be unaffected thereby; while all venoms are rapidly destroyed by pancreatic digestion.

Freezing does not affect the various kinds of venoms, but they are all profoundly modified by being heated at a temperature between 75° and 80° C. Of late much attention has been called to the resemblance between the formation of snake-venom, and the production of the poisons by the diphtheria bacillus, anthrax bacillus and tubercle bacillus on the one hand, and the products of gastric and pancreatic digestion on the other.

In all these processes, various albumoses are formed, varying markedly in the degree of their toxicity, but all more or less poisonous if injected subcutaneously, while in some the process is carried still farther with the production of peptones.

As stated before, in the case of snake-poison the process of albumin-hydration probably stops short of this stage.

Another interesting point is that in some of these cases, notably gastric and pancreatic digestion, and digestion by the diphtheria bacillus, this conversion of the albumins into albumoses is brought about through the agency of a ferment or enzyme; while recently it has been suggested that in the formation of snake-venom, an enzyme may possibly take part.

TREATMENT OF SNAKE-BITE.

It is, however, regarding the treatment of snake-bite that most interest has centered during the past few years.

One has but to glance over the myriad medicaments used in this condition, drawn from the animal, vegetable and mineral kingdoms, to recognize how utterly unscientific and irrational has been the treatment of the great majority of cases, while many of the so-called remedies come directly from the realms of witchcraft and voodooism.

And yet in no condition more markedly than in this does the old adage "Bis dat, qui cito dat" hold good.

The prime object is to prevent the absorption of the poison, and if this can be done rapidly and efficaciously, we may get cures in cases in which a few minutes' delay or the wasting of time in useless procedures would inevitably result in death.

As to the best local treatment to be carried out, this varies somewhat according to the authority quoted, but the main principles are the same in all.

In the first place, a tight ligature should be applied above the bitten spot, if this is on the extremities, as we have seen is so in about 95 per cent. of cases.

As much of the poison as possible should then be removed, by scarification of the wound, excision in some cases, amputation, perhaps, if the bite is on a finger or toe and the species of snake a very dangerous one, tight bandaging from above and below toward the wound, cauterization of the bitten area, cupping or sucking the wound, although this last procedure is vigorously opposed by Fayrer and others.

About the wound should then be injected some one of the substances which experiments have shown to be rapidly destructive to the venom, usually by oxidizing it into harmless or less harmful substances.

For this purpose, potassium permanganate in solutions of from 1 per cent. to 5 per cent. as recommended by Blyth, Lacerda and Aron, and calcium hypochlorite or gold chloride as recommended by Calmette before he had developed his present method of treatment, are probably the best, although if these are not at hand, the caustic alkalies, bromine or chlorine water, carbolic, tartaric or chromic acids, tincture of iodine or even dilute solutions of mercuric chloride may be used.

Obviously all of the above-mentioned remedies are useless when the poison has once reached the general circulation, as none of these substances owe their efficacy to anything but their ability to destroy or oxidize proteids, or to form with them insoluble compounds, and would thus act equally destructively on the tissues of the body if injected into the system.

If the venom has reached the general circulation, besides hastening its elimination by washing out the stomach, and keeping the bowels and bladder well emptied (for it has been shown that the poison is, at least partially, excreted by the kidney), our energies should be devoted to counteracting as much as possible the constitutional effects of the poison, by the use of appropriate means.

Probably lives have been saved by these means, especially

after bites by the less venomous species of snakes, but according to Fayrer, all treatment is practically useless in those cases in which a member of the Indian Thanatophidia has injected its full quantity of poison into its victim, and local treatment has not been immediate. Among the remedies which have been most used to attempt to counteract the poison's constitutional effects, may be mentioned alcohol, ammonia and strychnia.

From time immemorial, alcohol has been used in this condition for its stimulating effect, while it has only been comparatively recently that ammonia has been given in any other way than by the mouth.

Due to Halford's experiments, large doses—as much as 1 drachm of the liquor ammoniae fortior—were given hypodermically, but later work has shown the utter uselessness of this drug as an antidote.

The same is largely true of strychnia, recommended first by Pringle in 1868, and more recently, in 1889, strongly advocated by Mueller, who regarded it as a true antidote if given in such large doses as to cause constitutional effects; three years later, however, indisputable figures were brought forward to show that under this treatment the mortality had not been decreased in the slightest degree.

Although useless as antidotes, both these remedies and to a less extent alcohol are probably useful in mild cases in lessening the nervous and cardiac depression after snake-bites.

Because of the marked effect of snake-venom upon the respiratory apparatus, artificial respiration has been tried in a few cases, but although the life of the man or animal is prolonged by this means, no case has been reported in which life has been saved.

Encouraged by the rapid development of the subject of serum-therapy, and by the successful results obtained in many cases, notably diphtheria and tetanus in combating by sera the effects of the toxines of bacterial growth, certain investigators, notably Calmette, at the Pasteur Institute in France, and Fraser, in Great Britain, have turned their attention to the preparation and properties of antivenomous serum, and the possibility of making use of it as a curative agent.

In 1887, however, Sewall, in the United States, first showed that a certain degree of tolerance to rattlesnake poison could be obtained by frequently feeding animals on small doses of the venom.

The results obtained by Fraser and Calmette have been quite markedly different, while their views regarding the mode of action of the antivenomous serum are almost diametrically opposed to each other, Fraser believing in the specificity of the various venoms and sera, i. e., from a serum which might immunize against one species of snake, much less good results could be expected in the case of poisoning by snakes of other species; while Calmette thinks that the active principle in the poisons of all snakes, and even of poisonous lizards and scorpions is the same, i. e., a serum which would immunize against one variety of very poisonous snake would immunize equally well against all other varieties.

All recent observers are agreed that an animal or person can be vaccinated against what would otherwise prove a fatal dose by the subcutaneous introduction of small, repeated doses of the poison.

But the reasons for this cause discussion—Fraser and Phisalix believing that the protection or immunity is chiefly due to the accumulation in the blood of an antidotal substance, which originates, at least in part, from the venom, and is normally one of the constituents of the poison itself; while Calmette, in direct opposition to this, believes that the antidotal substances are formed in the blood of the vaccinated animal itself by a certain reactive process of the organism.

Fraser, in Great Britain, and Cunningham, in India, found that the antidotal results obtained by using the serum of vaccinated and immunized animals were only of a high degree in the cases of injection of the poison of the *same* species of snake; the latter, among his other conclusions, stating that "blood-serum of vaccinated animals is efficacious as an antivenom, but only against the poison which comes from the same species of snake."

Kanthack, in this connection states that, although most snake-poisons belong to the same physiological group, and yield to the same antidote, nevertheless Calmette's serum prepared against Cobra-venom, has no effect upon Daboia-venom.

According to Fraser's experiments, it would take 300 cc. of the strongest rabbit-serum that he could produce to save the life of an average-sized man who had been bitten by one of the most venomous variety of snakes—an amount so great as to practically destroy the possibility of its practical application. Fraser, also found that the bile of poisonous snakes, and to a much less extent the bile of innocent snakes, of oxen and of guinea-pigs possessed antidotal properties, but here again the bile was much more effective against the poison of that variety of snake from which the bile was obtained; he also states that the serum of venomous serpents likewise possesses some antidotal properties, but Phisalix and Bertrand have described this as a process of vaccination, unless the blood-serum be heated to 60° C., when a true antidote is formed.

This is of especial interest because both snake-blood and snake-bile are very important remedies in the armamentarium of the native Hindoo snake-charmer and doctor, and too many well authenticated stories exist, showing immunity and cure to make it at all doubtful that these persons possess methods of treatment which are doubtless of value. The rationale of these experiments of Fraser's in regard to the antitoxic action of the bile is, of course, directly derived from the oft-repeated observation that the venom, unchanged in the stomach, is rendered rapidly inert after entering the duodenum, Fraser therefore regarding it as likely that the bile played some important part in this destruction or neutralization.

As bile is itself poisonous, Fraser isolated from the bile a non-toxic substance which had marked anti-venomous properties, and suggested that this might possibly be used for curative purposes outside the laboratory.

He also found that by feeding animals upon snake-poison, an immunity could be produced which would last 4 to 5 days; as however, at least 2 hours are required to establish this immunity after the feeding, the result of this experiment can be of no practical value.

Calmette, at the Pasteur Institute at Lille, France, has been carrying on experiments upon snake-venom exactly analogous

to those upon the toxines of tetanus and diphtheria, at first using small animals, but of late making use of larger animals, especially horses, in the preparation of his antivenomous serum. In July, 1896, his results had been attended with such success that he presented them to the Royal College of Physicians and Surgeons in London. These experiments were designed to show both the preventive and curative powers of his serum, and were as follows:—

(1) The lethal dose of cobra-venom being found to be 1 milligramme of dried substance (subcutaneously administered), which will kill a rabbit in 12 hours, or 2 milligrammes will kill in 16 to 17 minutes, 3 c. cm. of the protective serum was injected, and 6 hours later, 2 mg. of the dried venom; no symptoms occurred in these immunized rabbits, while control animals died in 16 and 17 minutes respectively.

(2) A second series was given 5 mg. of the dried venom subcutaneously, and one hour later 3 c. cm. of the antivenomous serum; all remained well.

(3) In a third series, 3 c. cm. of the antitoxine were injected one-half, one and one and a half hours after the injection of a fatal dose of the poison, and only in the last case (i. e., those injected one and a half hours afterwards) did the rabbits die.

All the animals that recovered in these experiments were perfectly well 8 days later.

The 1st experiment was designed to show the preventive, the 2d and 3d to show the curative powers of the serum.

In concluding another article on the same subject, Calmette says:—"Animals may be immunized against the venom of serpents either by means of repeated injections of doses, at first feeble, and becoming progressively stronger, or by means of successive injections of venom mixed with certain chemical substances, among which I may especially mention the chloride of gold and the hypochlorites of lime and soda; the serum of animals thus treated is at the same time preventive, antitoxic and therapeutic, exactly as is that of animals immunized against diphtheria and tetanus."

Calmette studied the venom of the following reptiles: Naja tripudians, Crotalus durissus, Bothrops lanceolatus, Naja haje, Cerastes, Bungarus fasciatus, Pseudechis, Hoplocephalus curtus, H. variegatus, Acanthophis antarcticus, Trimeresurus viridis and Trigonocephalus contortrix.

Although all these venoms have their well marked toxic peculiarities and produce their various local phenomena, nevertheless animals immunized by vaccination against very large doses of any of these venoms, resist likewise inoculations of very powerful doses of the venom of any one of the other serpents mentioned, according to Calmette.

This belief in the non-specificity of the toxines and antitoxines of snake-venom is shared by other investigators on the same subject, as Wehrmann.

In this connection it is interesting to note some of the discoveries in the field of serum-therapy that have a suggestive bearing upon this point.

Marmorek has shown that animals immunized against anthrax or tetanus furnish a serum antitoxic to snake-venom; also that dogs immunized to a high degree against rabies are capable of great resistance to snake-poison; while Calmette and others have shown that rabbits vaccinated against snake-venom, become resistant to poisoning by abrine, while those vaccinated against abrine may in turn acquire a certain degree of immunity against snake-venom, diphtheria, ricine or even sometimes against anthrax, and animals vaccinated against erysipelas or rabies may possess a serum that may even be preventive against snake-venom.

Calmette is violently opposed to the idea that there is a chemical neutralization of the toxine by the antitoxine, he regarding the immunity as due to a certain "insensibilization" of the cells in respect to the venom, which is conferred upon them for a short time by the antitoxine.

In support of this, he showed by experiment that if a lethal dose of venom and a corresponding dose of anti-venomous serum be mixed in a test-tube and injected into an animal, there are no injurious effects; while if the mixture, after standing for a sufficient length of time to bring about any chemical reaction if it should take place, be heated to 70° C. (at which temperature the antitoxic serum loses its efficacy) and then injected, death occurs as if the animal had received no antidote whatever.

Recent experiments suggest that some, at least, of the immunity after antivenomous serum has been injected, may be due to increased powers of phagocytosis towards the toxine on the part of the leucocytes.

Whatever may be our views as to the specificity or non-specificity of toxine and antitoxine, nevertheless the practical results obtained from the use of the serum give promise of great success.

For the past two and a half years, the Pasteur Institute at Lille, has been sending out serum of a high immunizing power to various parts of the world where snake-poisoning is frequent, and already has received reports showing favorable results in persons that have been bitten by the following varieties of venomous snakes: (1) Naja tripudians (cobra) of Indo-China, (2) Bungarus ceruleus (krait) of India, (3) Naja haje (asp) of Egypt, (4) Naja noir of West Africa and (5) Bothrops lanceolatus of Central America, although Martin has so far been unable to get such good results in those bitten by the Australian snakes.

It may be of interest to report one of these cases more in detail.

A boy working in the laboratory at Lille, while carelessly opening a box of newly arrived snakes, was bitten on the hand; almost immediately symptoms of violent intoxication set in, and in an hour, besides the swelling and oedema, there was insensibility of the hand and forearm, great pain in the upper arm, neck and axilla, and nausea.

12 c. cm. of the serum were injected and immediately the symptoms commenced to subside, and by the next day the boy was practically well. A woman who happened to be bitten by the same lot of snakes died in 2 hours, untreated.

Incidental to the more practical side of his work, Calmette has made a number of other interesting observations: For instance; vaccinated rabbits remain immune for a considerable length of time, losing their immunity the more rapidly, the more quickly they have become immunized; the female rabbit is able to transmit her immunity, provided the gestation takes place at the height of the immunizing period, the young

retaining this immunity for about 2 months; on the other hand the immunized male rabbit is unable to transmit his immunity to his offspring.

Even from the short account that I have given, it will be seen that decided advances have been made during the past few years, in our knowledge of the nature of snake-poison, while the number of favorable reports of the use of the anti-venomous serum makes it probable that a real antidote to snake-poison has at last been found.

In an article as brief as this, it is impossible to more than touch lightly upon the many interesting points in connection with snake-venom and snake-bite, but if any one cares to delve more deeply into the subject, I would refer him to the comprehensive articles of Mitchell, Fayrer, Lauder-Brunton, Calmette, Fraser, Kanthack, Martin, Cunningham and Wall, in whose pages he will find much that will prove of interest to the student of natural history, of toxicology, of chemistry, and of medicine and therapeutics.

THE MENSURATION AND CAPACITY OF THE FEMALE BLADDER.

OBSERVATIONS ON THE FEMALE BLADDER DILATED BY ATMOSPHERIC PRESSURE IN THE KNEE-BREAST POSTURE.*

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[The investigations here reported were undertaken by the writers upon the suggestion and with the constant aid and direction of Dr. Howard A. Kelly, of the Johns Hopkins Hospital, to whom they take pleasure in acknowledging their indebtedness.]

The interest attaching to the work is both practical and scientific, for it concerns the gynecologist even more than the anatomist.

How little is really known about the bladder is found upon a cursory reading of the surgical and anatomical text-books containing their meager and contradictory statements. The measurements and capacity of the female bladder, given in the text-books, have been determined by *post-mortem* examination, by distention to discomfort by urine (or other fluids), and by other inexact methods, which have given imperfect and often contradictory results.

The methods employed by the writers in their investigation differ from those heretofore employed in essential and important respects:—1st, all measurements have been made on living women, in most cases with the bladder either perfectly healthy, or so slightly changed from the normal as not to affect the accuracy of the results; 2d, all examinations have been made with the women in the knee-breast posture, with the rectum, vagina and bladder all (with a few exceptions), dilated with air, according to the method so well known from the writings of Kelly. With all cases thus placed under similar conditions for the examination, the chief sources of avoidable error were removed, and relative measurements could be made and certain averages and standards found. It was, of course, impracticable to estimate the variations of intra-abdominal pressure in different cases or to fix upon a standard of this force, but repeated examinations of the capacity of the bladder in the same case showed that this force was nearly uniform. Although this force may be assumed to vary in different cases and thus to influence the capacity of the bladder when it is opened to the entrance of the outside air, still we believe that this variation is far less important than the variation due to individual tolerance or irritability to fluid distention, the method previously most generally employed in determining the capacity of the bladder. It was found, moreover, that by this method of air dilatation, no discomfort* was felt by the woman, and consequently no resistance, either voluntary or involuntary, was offered by her, thus adding to the uniformity of the conditions of observation. On the contrary, it was found that distention by fluid to discomfort was subject to the peculiar and varying irritability or tolerance of the subject, and thus gave no uniform basis of comparison.

The work was undertaken primarily to afford to the gynecologist some additional information on the size, shape, position, internal measurements, and capacity of the bladder, and incidentally to furnish the anatomist with some of the same data.

Had the study been made primarily from the anatomical viewpoint, it might have been better to have made the observations on the bladder alone distended, without the distention also of the vagina and rectum. But we have found that while the dilated vagina and rectum have a certain influence on the shape and position of the dilated bladder, they influence only slightly its air capacity.†

The chief points investigated were, 1st, the average atmospheric distention capacity of the female bladder, and 2d, its actual internal measurements, from the internal urethral orifice to certain chosen points on its walls.

For the purpose of the first study, the woman was put in the knee-breast posture and the three pelvic cavities were each allowed to dilate with air. A closely fitting catheter was then introduced into the bladder, attached at its

*Abbreviated report of the paper read before the Johns Hopkins Medical Society, December 4, 1899. The full report will appear in the Journal of the American Medical Association, December 16, 1899.

*The patients never complained of discomforts from the distended bladder while in the knee-breast posture. After rotation to the dorsal position, however, they usually felt some slight discomfort, if they were not under anæsthesia, and were instructed, before being rotated, to refrain from any expulsive effort.

†This last statement needs confirmation, as our observations on this point were few.

external end to a long, soft rubber tube. The rubber tube was closed by a clamp and the woman was then rotated carefully by assistants from the knee-breast into the dorsal position. The rubber tube was then introduced into a deep vessel of water and from below upward into an inverted glass graduated cylinder completely filled with water, and was held pointing upward in this position by an assistant. The clamp on the tube was then released, and the entire air content of the bladder was expressed by the ordinary gynecological bimanual method, with one hand exerting pressure on the bladder externally from the abdominal wall and with the other hand pressing at the same time upon the bladder from within the vagina or rectum.

The air thus expressed was collected in the glass cylinder, displacing from above downward an equal amount of water, and the amount was read off on the graduated cylinder, thus determining the exact air capacity of the bladder.

To test whether all the air was thus removed from the bladder, a special instrument was devised, consisting of a double-barreled catheter (Figs. I and II), by which the bladder, after bimanual expression, was flushed with boric solution, and any air remaining in it was forced out and collected for measurement. It was thus found that bimanual expression had been effectual and complete, and practically all the air in the bladder had been removed.

In the 25 women examined the average bladder capacity by atmospheric dilatation was found to be 303 cc , individual cases ranging from a minimum of 160 cc. to a maximum of 545 cc.

Measurement was also made in 22 cases of the fluid content of the bladder, boric solution being used for this purpose. On anæsthetized cases the solution was introduced through the double-barreled catheter until it overflowed through the upper barrel, on the cases without anæsthesia, until discomfort was caused to the woman. The average fluid capacity was thus found to be 429.7 cc., varying in individual cases from a minimum of 210 cc. to a maximum of 840 cc. The fluid capacity of the bladder was thus found to be more than one-third greater than the air capacity, a difference that would be expected, because of the elasticity of the bladder-walls under the increased pressure of fluid.

With reference to the influence of anæsthesia on the capacity, the following table has been arranged:

	Atmospheric Capacity.		Fluid Capacity.	
With anæsthesia,	306.7 cc.	(average 17 cases.)	449.6 cc.	(average 15 cases.)
Without "	295.0 cc.	(average 8 cases.)	387.1 cc.	(average 7 cases.)
	303.0 cc.	(average 25 cases.)	429.7 cc.	(average 22 cases.)

From these figures it is seen, as might be expected, that the average capacity of the bladder for both air and fluid is somewhat greater with than without anæsthesia, explained, doubtless, by the relaxation of the bladder-walls during anæsthesia. The above figures tend also to show that this difference is greater with fluid than with atmospheric distention, due to the more varying irritability of the bladder, without anæsthesia, to fluid distention.

The influence of child-bearing on the capacity of the bladder is shown in the following table:

	Atmospheric Capacity.	Fluid Capacity.
Nulliparous,	318.8 cc. (average 13 cases.)	464.5 cc. (average 11 cases.)
Parous,	291.2 cc. (average 12 cases.)	395.0 cc. (average 11 cases.)

The explanation of these figures, showing the greater capacity of the bladder of nulliparæ, is doubtful, and it may be that it is purely accidental, due to the limited number of cases observed. We would suggest, however, that it may be due to the greater elasticity of the bladder of the nullipara, influenced both by her younger average age and by the fact that her bladder and the surrounding tissues have not suffered injury and undergone sclerotic changes as the result of the pressure of the gravid uterus. The influence of age is shown in the fact that the average age of the women who had borne children was 36 years, and of the nulliparous women only 26 years.

The second chief object of this study was to gather some statistics on the internal mensuration of the bladder under atmospheric dilatation in the knee-breast posture. The value of such measurements to the gynecologist is apparent, but they have not before been accurately ascertained.

The distance of certain points from the internal urethral orifice was measured. The points chosen were:

(1) The *vertex*, or summit, the most prominent and distant point in the concavity of the upward and anterior bulging of the ventral wall, placed usually well above the reflection of the peritoneum and the departure of the urachus; (2) the most prominent and distant point in the upward and dorsal bulging of the *posterior wall.* This point is found a few centimeters above the peritoneal reflexion, and is usually opposite the end of the cystoscope when it is held in the axis of the patient's body. Quite frequently, however, the cystoscope must be directed more posteriorly to bring this point into view; (3) the point of greatest outward bulging in the *left lateral wall;* and (4) the point of greatest outward bulging in the *right lateral wall.*

These four points are not scientifically fixed points, but in actual work are found to be sufficiently clearly indicated for practical purposes of identification and description (Fig. III).

The average measurements obtained for these four points were, to

Vertex.....	7.14 cm.	Left lateral wall..	6.70 cm.
Posterior wall.....	5.77 cm.	Right lateral wall.	5.92 cm.

Taking the measurements separately for nulliparous and for parous women, the averages are found to be:

	Vertex.	Posterior wall.	Left lateral wall.	Right lateral wall.
Nulliparous (average, 13 cases)	7.43 cm.	5.75 cm.	7.03 cm.	6.12 cm.
Parous (average, 12 cases) ...	6.83 cm.	5.79 cm.	6.35 cm.	5 72 cm.

The greater average internal dimensions of the bladder of nulliparæ, here shown, correspond to the greater capacity for air and fluid, as already pointed out, and may be explained in the same way.

The asymmetry of the dilated bladder shown by the unequal lateral measurements is of interest. In sixteen cases the left lateral measurement is greater than the right, the reverse is true in six cases, and in three the left and right internal lateral

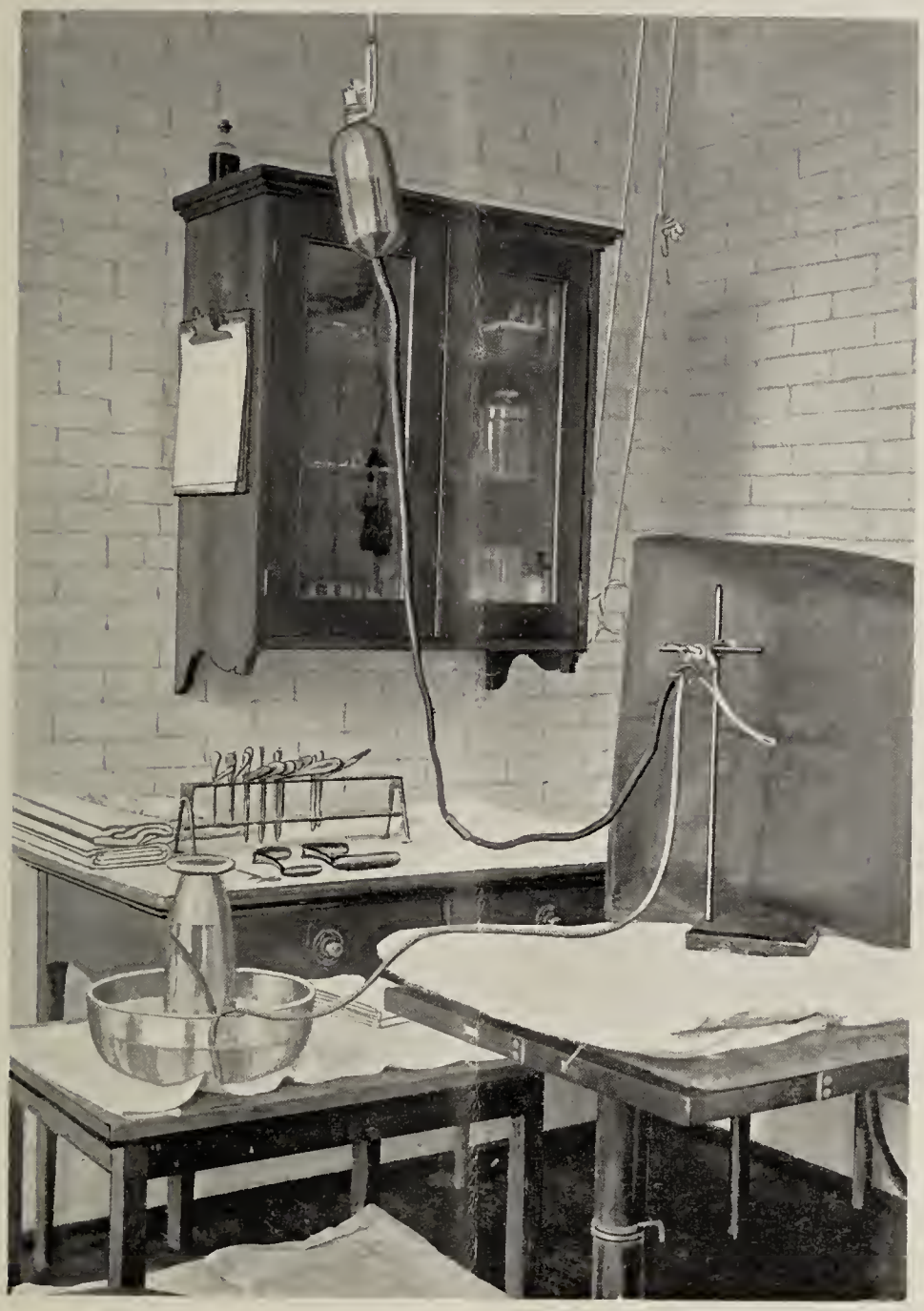


FIG. I.

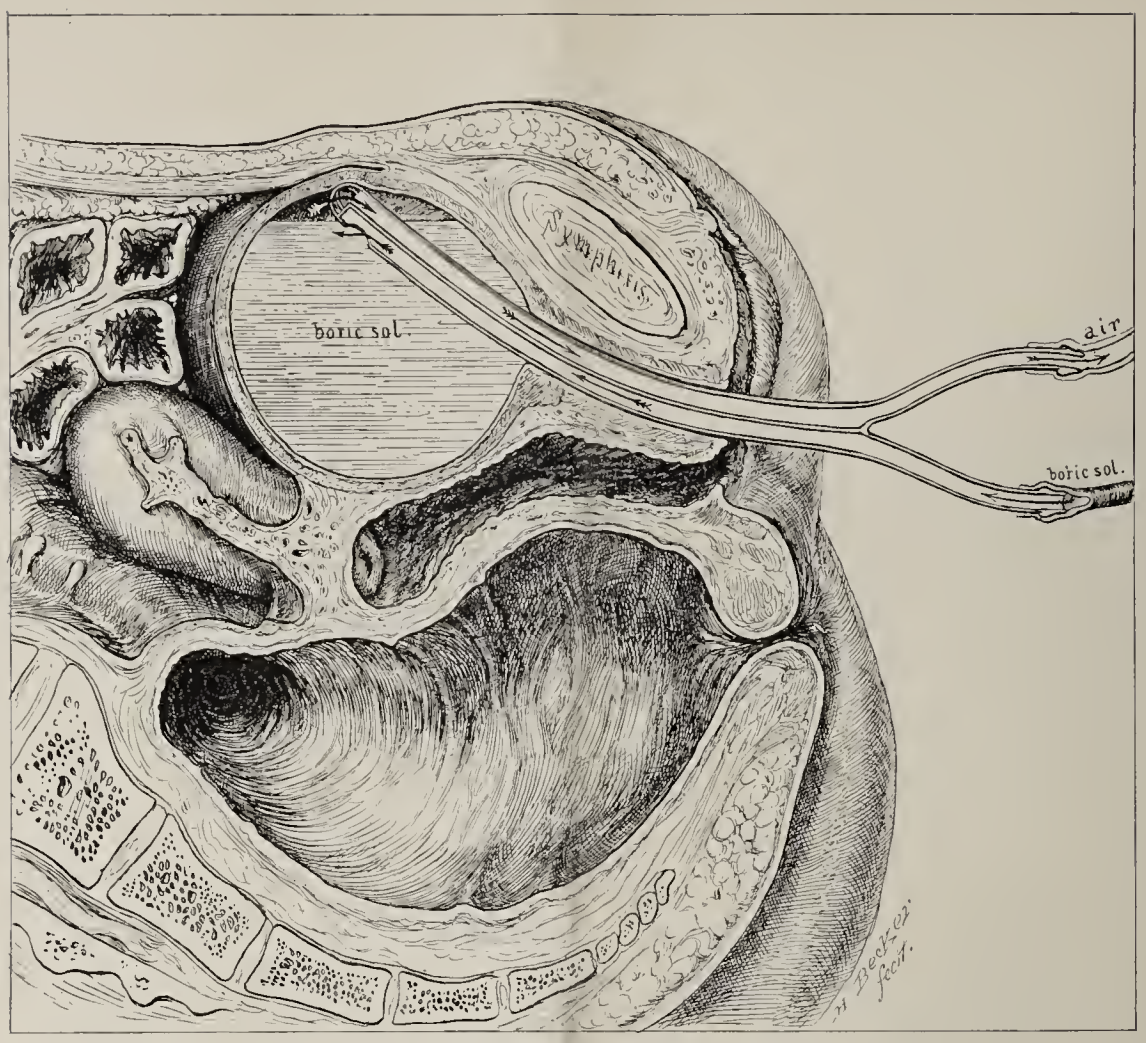


Fig. II.

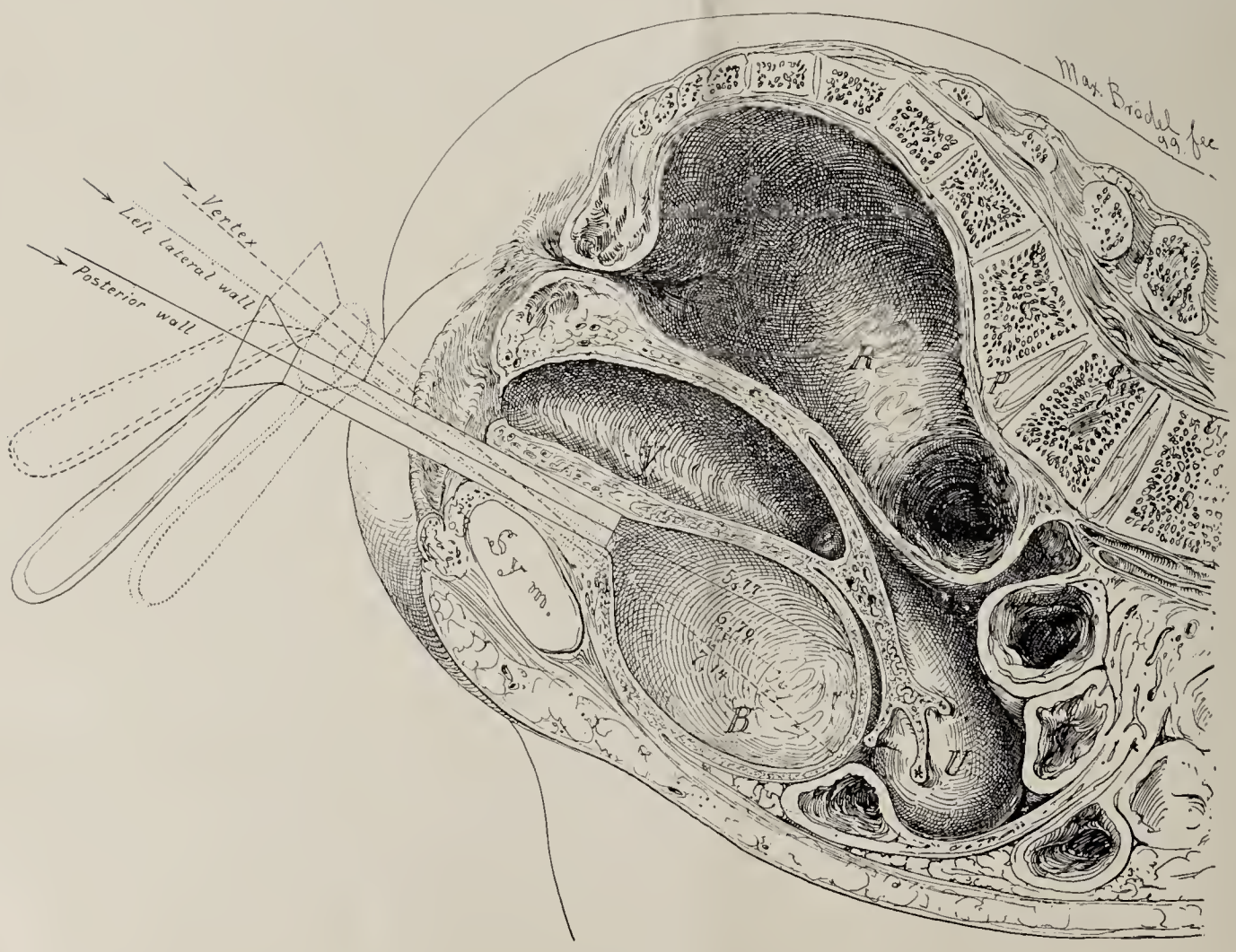


Fig. III.



Fig. IV.

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measurements are equal. The occasional asymmetrical position of the bladder has been noted by anatomists, but never before has this asymmetry been recorded in so large a proportion of cases. This tendency of the bladder to be placed more to the left than to the right, at least when the patient is in the knee-breast posture with the three pelvic cavities dilated with air, may be explained by the fact that the rectum in women is found more commonly on the right than the left in the pelvis, and thus the distended rectum tends to displace the bladder toward the left. Our observations on the position of the rectum in women are directly opposed to the usual statements of the text-books of anatomy. Mr. Max Brödel,* artist to the gynecological department of the Johns Hopkins Hospital, whose observations on the anatomy of the organs of the pelvic cavity have been exact and extensive, informs us that his own experience confirms our observation on this point.

Another factor producing some slight asymmetry of the dilated bladder is the fact that the uterus† is usually placed somewhat to the left of the median line and encroaches upon the left upper posterior quadrant of the bladder, as is well shown in Fig. IV. The influence of this factor is to lower the point of greatest outward bulging of the left lateral wall, point (3), so that it is found to be at a lower level than point (4) on the right lateral wall.

It was found that the same patient examined repeatedly by the same method gave, as a rule, nearly uniform measurements, the variations being slight.

All cases were free from any constricting clothing at the time of the examination, and the rectum had been emptied by cathartic or enema before the examination.

With the patient in the knee-breast posture, and the rectum, vagina and bladder all dilated by atmospheric pressure, it was found that the true pelvis was always completely occupied by these three organs and that the bladder and the uterus tended to rise upward and forward. In multiparæ the uterus was found to be displaced so far upward and forward that its fundus could be felt within a few centimeters of the umbilicus (Fig. IV).

The ballooning of the rectum and vagina before the bladder was allowed to fill with air, was found to be of great importance to the ease of the examination of the ureteral orifices, in the fact that the dilated vagina and rectum press from behind upon the base of the bladder, thus bringing the trigonum and ureteral orifices forward and into easy view of the speculum. *Neglect of this point and failure to first allow the rectum and vagina to dilate are accountable in large measure for the difficulty found by many gynecologists in catheterizing the ureters.*

The ureteral orifices were seen on or were indicated by a slight elevation of the mucous membrane, the *mons ureteris* of Kelly, but in some cases in young nulliparous women the ureteral opening was indicated by a small round black point which was never observed in older women who had borne children.

The bladder as a whole, when dilated with air and observed during operation within the pelvic cavity (from abdominal section) was found to be ellipsoidal in form, flattened somewhat in its antero-posterior diameter, and increased transversely. The transverse diameter was always the greatest measurement.

A mathematical calculation of the cubic content of an ellipsoidal viscus of the dimensions of the bladder corresponds closely with the actual air capacity obtained by expression.

The average length of the urethra in seventeen cases was 3.3 cm., the shortest urethra measuring 2.7 cm., and the longest 4.2 cm.

It is hoped by the writers that the measurements and observations above recorded, though limited to twenty-five cases, may prove of interest and service especially to the gynecologist, by affording a certain amount of carefully ascertained facts about the relative measurements and topography of the female bladder under air dilatation in the knee-breast posture.

Description of Figs. I, II, III, IV.

Fig. I—Represents the double-barreled catheter and attachments, used for determining the residual air in the bladder, after bimanual expression.

Fig. II—Median section, dorsal position, showing the double-barreled catheter in position in the bladder, boric solution entering through the lower chamber and forcing the air out through the upper chamber.

Fig. III—Median section, knee-breast posture, showing the pelvic cavities dilated with air, and the cystoscope in position for obtaining the measurements of the vertex, posterior wall, and left lateral wall.

Fig. IV—Median section, knee-breast posture, showing the anatomical relations of the pelvic organs when the rectum, vagina and bladder are dilated with air. (Multipara.)

*To Messrs. Brödel and Becker, of the Johns Hopkins Hospital, we wish to express our indebtedness for their beautiful drawings from which Figs. II, III and IV have been made.

† This observation is also opposed to the statements of some text-books of anatomy, and is confirmed by Mr. Brödel.

SUMMARIES OR TITLES OF PAPERS BY MEMBERS OF THE HOSPITAL AND MEDICAL SCHOOL STAFF APPEARING ELSEWHERE THAN IN THE BULLETIN.

Howard A. Kelly, M. D. Exploration of the Abdomen as an adjunct to every Celiotomy.*

I had occasion on several instances some sixteen years ago to make a post-mortem examination and to remove various viscera which I was desirous of inspecting, through the vaginal vault in women and the perineum and rectum in men. These experiences showed me that it is easy to reach all the viscera through an incision as far as possible from the centre of the abdomen, large enough to admit the forearm, and suggested the propriety or rather the necessity of making a somewhat analogous investigation of all the abdominal organs in the living subject every time the abdomen is opened.

The routine examination of the abdominal and pelvic viscera in all celiotomies, where it does not endanger the life of the patient,

*A more extended consideration of this subject appears in the *Medical News*, December 16, 1899.

will commend itself to a surgeon for a number of excellent reasons, some of which are the following:

First, as abdominal diseases are commonest in middle life, the period when most of our celiotomies are performed, it is practically certain that the coincidence of two or more entirely independent diseases will be discovered in some instances by means of this examination.

Again, there is a constant association between certain abdominal affections and affections elsewhere, in the form of a mutual interdependence, either from the propagation of disease, as in the case of cancer, sarcoma and tuberculosis; or mechanically, where the effects of pressure are manifested near to or at a distance from the seat of disease, as in the case of pelvic tumors or inflammation obstructing the vascular, the urinary or the alimentary channels. These secondary conditions often in their initial and curable stages may be brought to light by the method of investigation here advocated.

Moreover, such an examination, if negative, gives both operator and patient a much more comfortable assurance that the convalescence will be without interruption, as well as the satisfaction of realizing that there is no visceral affection in progress which may in the near future tend to shorten life or to impair health.

The following diseases are most likely to be found in such a routine examination: appendicitis, hernia (either inguinal or umbilical), hydroureter, disease of the omentum, pyloric cancer, movable kidney, enteroptosis, cancer of the liver, perihepatitis, gall stones.

In making the exploration extreme care must be taken to maintain asepsis by thoroughly sterilizing the arm or, better still, by wearing a rubber glove with a long sleeve reaching as far as the elbow. If the area in the immediate neighborhood of the incision is so septic as to require the use of drainage, the operator had best forego the more extended examination. The best position of the patient for the examination is either lying flat on the table or with the pelvis slightly elevated. The structures are examined in an order which must vary with the location of the incision. When the abdominal opening is made low down over the middle of the pelvis, I commonly follow some such routine as this: After carefully noting the condition of each pelvic viscus, uterus, tubes and ovaries, bladder and rectum, I look at the inguinal and umbilical ring and if there exists a hernia I proceed to sew it up at once from the inside of the abdomen. The next point of importance requiring examination is the vermiform appendix.* This should be removed if it shows any traces of previous inflammation. Then follows the inspection of the ureters, of great importance in gynecological operations. Every surgeon should be thoroughly familiar with the ureteral landmarks. The position of the transverse colon and the stomach is noted on account of the frequency of enteroptosis.

The operator now introduces his forearm and palpates both kidneys, noting their presence, size, form and mobility. A stone in the renal pelvis is readily felt. After the kidney, the liver is palpated, its apparent size, the regularity of its surface, any adhesions, which when present indicate perihepatitis, being noted, and most important the gall bladder is explored. I next put my index finger in the foramen of Winslow and trace the common duct down for several centimetres, feeling for stone.

The spleen, the pancreas, retroperitoneal lymph glands, and finally the abdominal portion of the aorta are palpated in order.

There are in general three classes of cases to which this extended examination may be applied.

First. Those in which there has been no reason to anticipate disease of any other organ and the examination is made simply as a routine procedure whenever it adds nothing to the gravity of the situation.

Second. Those cases in which, on opening the abdomen, contrary to expectation, no disease is found near at hand. I recall a case* of this sort in which I made an incision over the appendix, and, finding no appendicitis, enlarged the opening and discovered a gall stone within a ruptured gall bladder; also an instance in which gall stones were believed to be present, but on finding the diagnosis at fault, I introduced my arm through the enlarged incision and came upon a large hematoma of the ovary.

Third. The group of cases in which there exists a definite percentage of chances that the disease discovered at the time of operation is complicated by the affection of some other organ neighboring or remote.

* The method I follow in reaching the various organs is detailed in loc. cit.

Reid Hunt. Direct and Reflex Acceleration of the Mammalian Heart with some Observations on the Relations of the Inhibitory and Accelerator Nerves.—*American Journal of Physiology*, II, pp. 395-470.

Experiments on dogs and cats showed that in these animals the center of the accelerator nerves is almost always in a condition of tonic activity and that the normal rate of the heart is determined in part by this tonic activity. Section of the accelerator nerves sometimes causes the heart to become irregular; this is especially true if the irritability of the heart is low. The most important functions of the accelerators seem to be connected with their tonic activity.

Long-continued stimulation of the accelerators causes fatigue and sometimes even death of the heart. If the vagi are in tonic activity, or if they are stimulated simultaneously with the accelerators, the latter cause less fatigue of the heart.

Reflex acceleration might be caused either by increasing the activity of the accelerators or by decreasing the tonic activity of the vagi. The latter was found to be the usual if not the exclusive method. Reflex acceleration was never obtained after section of the vagi although the accelerators were intact, but was readily obtained if the vagi were intact although the accelerators were cut.

It seems very probable that most cases of rapid heart action (voluntary acceleration, acceleration during muscular exercise and after the administration of drugs, the rapid heart of paroxysmal tachycardia etc.) so far as they are dependent upon the extracardiac nerves, are largely due to diminution of the tonic activity of the vagi and not to a stimulation of the accelerators; in paroxysmal tachycardia especially the entire course of the acceleration is markedly different from the effects of stimulating the accelerator nerves in animals.

W. S. Baer, M. D., P. M. Dawson, M. D., and H. T. Marshall, M. D. Regeneration of the Dorsal Root Fibres of the Second Cervical Nerve within the Spinal Cord.—*Journal of Experimental Medicine*, January, 1899.

Lewellys F. Barker, M. B. Progress of Neurology.—*Philadelphia Medical Journal*, January 28 and February 4, 1899.

——— A Case of Glioma of the Lower Cervical Region of the Spinal Cord Producing a Total Transverse Lesion, in which there was Spasticity of the Lower Limbs and Persistence of the Deep Reflexes. A Study of a Peculiar Form of Degeneration (Degeneratio Micans) met with in this Case.—*American Journal of the Medical Sciences*, Vol. 117.

Simon Flexner, M. D. Some Points in the Pathology of Syringomyelia.—*American Journal of the Medical Sciences*, Vol. 117.

——— Hodgkin's Disease.—*American Journal of the Medical Sciences*, Vol. 118.

Thomas B. Futcher, M. B. Lipemia in Diabetes Mellitus.—*The Journal of the American Medical Association*, Vol. 33.

——— A Critical Summary of Recent Literature Concerning the Mosquito as an Agent in Transmission of Malaria.—*American Journal of the Medical Sciences*, Vol. 118.

* For description of cases, see loc. cit.

HENRY HARRIS, M. D. Preparation of the Abdomen for Operation. —*American Journal of Obstetrics*, Vol. 40.

HOWARD A. KELLY, M. D. A New Method of Treating Complete Tear of the Rectovaginal Septum by Turning Down an Apron into the Rectum and by Buried Suture through the Sphincter Muscle. (Illustrated.)—*Medical News*, Vol. 75.

—— New Handle and Grip for Scissors in Plastic and Other Work.—*American Journal of Obstetrics*, Vol. 40.

—— Operation for Complete Tear of the Perineum.—*American Journal of Obstetrics*, Vol. 40.

—— The Reflux of Air into the Ureters through the Air-Distended Bladder in the Knee-Breast Posture.—*American Journal of Obstetrics*, Vol. 40.

—— Some New Instruments to Facilitate the Operation of Myomectomy.—*American Journal of Obstetrics*, Vol. 40.

—— The Use of the Renal Catheter in Determining the Seat of Obscure Pain in the Side.—*American Journal of Obstetrics*, Vol. 40.

J. H. MASON KNOX, JR., PH. D., M. D. On Supra-arterial Epicardial Fibroid Nodules.—*The Journal of Experimental Medicine*, March, 1899.

JOHN BRUCE MACCALLUM, M. D. A Contribution to the Knowledge of the Pathology of Fragmentation and Segmentation, and Fibrosis of the Myocardium.—*The Journal of Experimental Medicine*, May-July, 1899.

FRANKLIN P. MALL, M. D. Liberty in Medical Education.—*Philadelphia Medical Journal*, April 1, 1899.

JOSEPH LONGWORTH NICHOLS, M. D. A study of the Spinal Cord by Nissl's Method in Typhoid Fever and in Experimental Infection with the Typhoid Bacillus.—*The Journal of Experimental Medicine*, March, 1899.

EUGENE L. OPIE, M. D. A Case of Hæmochromatosis. The Relation of Hæmochromatosis to Bronzed Diabetes.—*The Journal of Experimental Medicine*, May-July, 1899.

WILLIAM OSLER, M. D. An Acute Myxœdematous Condition, with Tachycardia, Glycosuria, Melæna, Mania and Death. *The Journal of Nervous and Mental Diseases.*

—— In Memoriam William Pepper. *Philadelphia Medical Journal*, March 14, 1899.

—— The Cavendish Lecture on the Etiology and Diagnosis of Cerebrospinal Fever.—*The Boston Medical and Surgical Journal*, Vol. 141.

—— The Clinical Features of Sporadic Trichinosis.—*American Journal of the Medical Sciences*, Vol. 117.

—— The Diagnosis of Typhoid Fever. A Discussion at the New York State Medical Association, October 25, 1899.—*New York Medical Journal*, Vol. 70.

OTTO G. RAMSEY, M. D. The Early Use of Purgatives after an Abdominal Section.—*American Journal of Obstetrics*, Vol. 40.

H. O. REIK, M. D. The Sterilization of Instruments with Formaldehyde.—*Philadelphia Medical Journal.* February 4, 1899.

W. S. THAYER, M. D., and JESSE WILLIAM LAZEAR, M. D. A Second Case of Gonorrhœal Septicæmia and Ulcerative Endocarditis with Observations upon the Cardiac Complications of Gonorrhœa.—*Journal of Experimental Medicine*, January, 1899.

J. WHITRIDGE WILLIAMS, M. D Anti-Streptococcus Serum.—*American Journal of Obstetrics*, Vol. 40.

—— A Case of Spondylolisthesis.—*American Journal of Obstetrics*, Vol. 40.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Monday, November 20, 1899.

The meeting was called to order by the President, Dr. Henry M. Thomas.

Cases Illustrating Forms of Pigmentation of the Skin.—Dr. OSLER.

CASE I. *Addison's Disease.*—A man, aged 40, was admitted a few days ago, complaining of weakness, pain in the stomach and bowels, and a gradual pigmentation of the skin. He had been a man of good habits and of good health until five years ago, when he began to have gastric trouble, chiefly regurgitation of the food. About four years ago he began to have pains below the costal margin and radiating over the abdomen. They came on in paroxysms three or four times in the course of the year, and were sometimes accompanied by vomiting. During this time his complexion grew steadily darker, and within the past twelve months his condition has grown worse. He has paroxysms of sudden pain, chiefly about the right costal margin, followed by vomiting, headaches and at times great prostration. These paroxysms are preceded by twitchings of muscles of the limbs, especially of the arms, so marked that he has not been able to write. After these spells the prostration is extreme and at times he has hardly been able to move in bed for nearly a week. Each spell leaves him weaker and he has not done a day's work for a year. The vomiting has averaged once a day during the past year, and yet his appetite is excellent. He has never had any diarrhœa. He looks somewhat emaciated and has lost fifteen or twenty pounds. The face, hands, and more particularly the body, are uniformly pigmented. There is slight pigmentation of the mucous membrane of the gums. His pulse is slow but not feeble and the blood count shows 6,000,000 red cells.

The combination of symptoms presented by this man is characteristic of Addison's disease, yet the case is somewhat peculiar. There is no history of tuberculosis; there is no reaction to tuberculin, and the duration of four or five years is rather unusual, the disease being as a rule very much shorter. Asthenia, such as he describes, a prostration of such a degree as to render him unable to turn in bed, or even to move, is most characteristic, and in fact the diagnosis may sometimes be made on the asthenia and gastro-intestinal symptoms without pigmentation.

CASE II. *Hæmachromatosis* (?).—This lad presents a still more remarkable and very much more unusual condition. This boy came here in April, 1896, with malaria and looking as if he had had a malarial cachexia of long duration. He had not been ill long, but looked so bronzed and pigmented

that we commented upon it in the history. We could not reasonably explain this pigmentation, but thought he must have had malaria longer than shown by his history. He came to the hospital again in February, 1897, with tertian malaria, and he was this time even more pigmented, but I forget whether at that time we noted any enlargement of the liver. In September, 1899, he appeared again with an acute psoas abscess, and at that time we found that he had an enlarged liver and spleen. Meantime we had been educated at the Society by Dr. Eugene L. Opie on the subject of hæmachromatosis, and this case corresponds in certain features with that remarkable disease. He has had no asthenia, no feebleness of pulse or muscular weakness, and no trace of gastro-intestinal disturbances, though those features have been sought for very carefully.

His pigmentation, as you see at present, is extreme, being quite marked in the face, and there is a little pigmentation of the mucous membrane at the margin of the lips. This bronzing has grown gradually deeper, so that he looks to-day more bronzed than he was in September. The liver is moderately enlarged and can be felt two or three finger breadths below the costal margin. The edge of the spleen is only just palpable. There is no sugar in the urine. Very possibly the condition is that of hæmachromatosis.

We have had a case of this remarkable disease which is characterized by progressive pigmentation of the skin and internal organs with hypertrophic cirrhosis of the liver, sclerosis of the spleen and finally of the pancreas with the pancreatic form of diabetes. The majority of these cases have been described under the name of Bronzed Diabetes. The disease was fully described by Dr. Opie in the last number of the *Journal of Experimental Medicine.*

Case III. *Melanoderma in chronic myocarditis.*—We can not say that all cases of progressive pigmentation of the skin are either due to hæmachromatosis or to Addison's disease, for there are certain conditions, particularly certain forms of chronic heart disease, some cases of chronic nephritis, etc., in which pigmentation of the skin develops and increases, and occasionally is accompanied even by pigmentation of the mucous membranes.

This man has been under observation for several years, having been admitted first in January, 1891, and nine times since, always with the same symptoms—shortness of breath, extreme irregularity of the pulse, dilated heart and sometimes with slight swelling of the feet. He has chronic myocarditis and progressive pigmentation of the skin. His face has deepened in color and the general surface of the body is pigmented. There is no pigmentation of the mucous membranes and though he has had extremely feeble and irregular pulse, he has not had the asthenia which characterizes Addison's disease. He has no enlargement of the liver or spleen. A piece of skin was removed for examination by Dr. Opie, but we have not yet received his report.

The diagnosis between the pigmentation of the skin in Addison's disease and in hæmachromatosis can be readily made, as the pigment in the latter case is an iron containing one and is found in abundance in the skin and also in the cells of the sweat-glands.

Case IV. *Melanoderma in Anæmia Splenica.*—Dr. Osler then referred briefly to a fourth cure of pigmentation of the skin, at present in the private ward. The young man had enlarged spleen and anæmia of the chlorotic type and gradual pigmentation of the skin. Several of the cases of splenic anæmia which had been under observation of late years have presented an extreme degree of melanoderma.

A Case of Purulent Leptomeningitis Associated with Acute Endocarditis due to Infection with the Micrococcus Lanceolatus.—Dr. Futcher.

The specimens which Dr. Barker will show were interesting on account of the number of complications that developed during the clinical course of this case in the wards. The patient came into the hospital November 5, complaining of shortness of breath. There was nothing special in the past history of the patient, nor in the family history. Seven years ago the patient had an attack of rheumatism and he gave a history of severe headache lasting about six weeks previous to admission and so intense that he was totally incapacitated for work. During this time he had frequent chills believed to be of malarious origin. Two weeks before admission he developed severe shortness of breath, cough and expectoration of bloody sputum. Later he had marked œdema of the feet and some general anasarca. On admission he was in marked distress, quite dyspnœic, somewhat cyanotic and presented the physical signs of aortic and mitral insufficiency. The sputum was tenacious and tinged with bright blood, such as one sees in cases of lung infarction. There was an area of consolidation over the middle lobe on the right side with typical tubular breathing and a pleuritic friction rub extending into the axillary region. The heart symptoms persisted for several days, the temperature during this time being irregularly elevated, running as high as 101.5°. During his illness he complained of severe pain in the region of the spleen, and splenic infarction was diagnosed. Nothing of special importance happened until the night of November 12, when his temperature arose 7.5 degrees inside of eight hours. The next morning he was semi-unconscious and it was found that he had distinct rigidity of the arms and legs with exaggeration of the knee-reflexes. On the 16th Doctor Osler suggested lumbar puncture and 15 cc. of slightly turbid fluid were obtained, which showed typical lanceolate diplococci in large numbers, but none of them intracellular. This of course clinched the diagnosis. Two days later he developed a conjunctivitis, and smears from this secretion also showed the typical lanceolate diplococci. About 24 hours before death there was complete steaminess and opacity of the right cornea. He died on November 18, the temperature being 106.4° at the time of death.

It was suspected that we would find at autopsy chronic endocarditis, with a supervening acute endocarditis, an infarction of the middle lobe of the right lung as well as of the spleen and a pneumococcus meningitis.

Exhibition of the Organs.—Dr. Barker.

The organs from this case are of more than ordinary interest. The autopsy confirms in almost every point the clinical diagnosis. The body 170 cm. long was that of a strong individual, moderately emaciated. Rigor mortis was

well marked and there was livor mortis in dependent parts. The peritoneal cavity was dry, and free from old adhesions. The diaphragm on the right side reached as high as the fourth intercostal space; on the left side to the fifth rib. There were a few firm old adhesions at the posterior margin of the left pleural cavity. On the right side the costal and visceral pleuræ were slightly adherent, especially over the middle lobe and the middle part of the upper lobe. The adhesions on the right side are all recent and fibrinous. This cavity is free from old fibrous adhesions. The pericardium aside from one old patch of thickening shows no alterations. The heart is much enlarged, weighing 418 grammes. In the right atrium the valve of the coronary sinus is remarkably developed, forming a large, thin, multiply perforated membrane. The cavities of the heart are somewhat dilated and the walls are thickened. On opening the left ventricle the bicuspid valve is found to measure 10.4 cm. in circumference. At the base of the anterior cusp of the valve on the atrial surface at its right extremity is a bulging area measuring 12 x 7 mm. and protruding for a distance of from 3–4 mm. above the surface of the valve, showing the endocardium before it. On puncture yellowish-green pus exuded and the swelling disappeared. The posterior cusp is shorter than normal, but otherwise shows no alterations. On the ventricular surface of the anterior cusp close beneath the posterior semilunar valve of the aorta there is a small ulcerated area, the margins and base of which are necrotic. Fibrin is deposited upon the surface of the ulcer. The introduction of a probe shows direct continuity with the abscess described on the atrial surface of the valve. In the aortic semilunar valves there are both old and recent changes. The old alterations consist in the main of fusion of the adjacent edges of the posterior and right semilunar valves. The edges of the two valves corresponding to this fusion are very much thickened and the lunulæ have disappeared. The lunula on the left side of the posterior cusp is intact and normal, while that on the right side has disappeared, and the valve is much thickened and retracted below it. The left lunula of the right semilunar valve is present, but considerably thickened, while the right lunula of this valve has entirely disappeared and the main body of the valve close to it is thickened. The adherent valves are, in the region of the adhesion practically immobile, owing to formation of new connective tissue and partial calcification. This change in the valve must have caused a relatively high degree of insufficiency and a slight stenosis. In the left aortic semilunar valve there has been apparently no chronic change except for slight thickening of the edge of the lunula. On the ventricular surface of the valve, however, there is distinct evidence of recent acute alteration. Here one sees a large flat ulcer, 1 cm. in diameter, to which flakes of fibrin are adherent. On the aortic surface of the same valve there is also an area of necrosis with deposition of fibrin. The trabeculæ carneæ are more prominent than normal in the left ventricle. The endocardium, especially over the septum, is slightly roughened and granular. At the root of the aorta there are some reddish and yellowish patches, elevated, which on section, are of a yellow color and opaque. The myocardium is in general pale brown in color, and no areas of scarring myocarditis are visible to the naked eye. The left coronary artery shows a few patches of arteriosclerosis in the descending ramus and also in the circumflex ramus. The right coronary artery also contains patches of sclerosis.

In the middle lobe of the right lung there is a large hæmorrhagic infarction surrounded by an area of fresh consolidation. Coverslips from the consolidated area show large numbers of pneumococci. The acute fibrinous pleurisy apparently had its origin by extension from the consolidated region of the lung. The left lung is emphysematous along its anterior margin and at the apex. There is only moderate coal pigmentation. Both lungs show the typical changes of chronic passive congestion.

The kidneys show a slight degree of chronic diffuse nephritis, the capsule being somewhat adherent and the cortical substance diminished in amount. Frozen sections also show the changes of acute parenchymatous degeneration. In the organs of the abdomen there is little remarkable with the exception of the changes of chronic passive congestion and the existence of a small hæmorrhagic infarction at the inferior extremity of the spleen.

On removal of the calvarium the dura mater was found to be unusually adherent, but otherwise normal. The superior sagittal sinus contains in its anterior part a few decolorized blood-clots, evidently *ante-mortem*, loosely adherent to arachnoidal granulations which project into the lumen of the sinus. At the base of the brain the arachnoid is raised from the underlying pia by a collection of pus several millimetres in depth. The pus contains large numbers of encapsulated pneumococci and many empty capsules. The very purulent area extends from a point 10 cm. in front of the optic chiasm backwards as far as the middle of the ventral surface of the cerebellum, the breadth of the area averaging as much as 8 cm. Pus is also abundant in the Sylvian fossa concealing the blood-vessels. While the process is most marked at the base of the brain, it is by no means confined to it, for if one looks at the lateral surfaces they are found also to be more or less involved. The deeper sulci on the lateral surface contain visible pus, but over the gyri themselves very little pus is observable, although the vessels of the pia arachnoid are everywhere intensely congested.

On opening the spinal canal a small hole was found in the dura in the lumbar region corresponding to the lumbar puncture made during life. The internal surface of the dura is smooth and glistening and aside from slight capillary ectasis shows no alterations. The subarachnoid cavity of the dorsal surface of the lumbar part of the spinal cord contains in many places accumulations of pus. The areas where pus is visible vary in size, some being much larger than others. The whole dorsal surface of the cord is more or less bathed in yellowish green pus. The pus is especially abundant in the thoracic part of the cord, but there is also a considerable amount in the cervical region. The pial blood-vessels are everywhere markedly injected. The spinal nerves do not appear to be especially involved in the inflammation, but along the cerebral nerves pus can be easily followed. It was especially abundant in the course of the cochlear and vestibular nerves. The possibility of middle-ear disease was of course suspected, but both ears

were carefully opened and no evidence of a primary process there could be found. Pus could be followed along the left optic nerve into the orbit and the eye when removed showed a general purulent inflammation. Radiating from the point of entrance of the ophthalmic artery yellowish lines could be followed along the vessels between the retina and the chorioid coat. The vitreous body and the crystalline lens were turbid from infiltration with pus, coverslips from which showed large numbers of pneumococci and no other micro-organisms. The iris, cornea and conjunctiva were also acutely inflamed.

Anatomical Diagnosis: *Leptomeningitis cerebrospinalis purulenta; panophthalmitis purulenta acuta; endocarditis ulcerosa maligna; endocarditis valvularis chronica; hypertrophia et dilatatio cordis; arteriosclerosis aortæ et aa. coronariarum; infarctio pulmonis dextræ; pneumonitis et pleuritis acuta; pleuritis chronica adhæsiva; congestio chronica passiva; infarctio lienis; degeneratio parenchymatosa renum; nephritis chronica diffusa incipiens.*

As has been said the pneumococcus was found in the pulmonic infarction and the consolidated lung about it; in the purulent inflammation of the eye; in the purulent exudate in the brain and spinal cord, and in the ulcers and abscess on the valves of the heart. Dr. Harris recovered the coccus in cultures. It is of interest to trace the probable sequence of events in the case. The chronic valvular endocarditis doubtless dates back to the attack of rheumatism from which the patient suffered seven years ago. Resulting from the old endocarditis and aortic insufficiency came hypertrophy of the heart accompanied, doubtless at times, by dilatation of its chambers. The chronic passive congestion of the lungs and other organs is obviously the result of the cardiac disease. It is probable that the chronic circulatory disturbance and the changes produced by it in the organs, made the individual unusually susceptible to infection. The question arises which of the several local infections from which the man suffered was primary. The clinical evidence is in favor of a primary endocarditis with complicating meningitis. It seems to me impossible to say, however, from the autopsy findings alone which is primary, the meningitis or the endocarditis. The infarction of the spleen is easily explicable when one remembers the ulcerative endocarditis in the left heart. The infarction of the lung can scarcely be referred to the heart directly, for there is no acute endocarditis on the right side of the heart, nor did the cavities of the heart contain thrombi of any kind. The most probable explanation seems to me to be that of the thrombi which formed in the superior sagittal sinus of the brain and were very loosely adherent, one passed into the venous current and by way of the right heart entered the pulmonary artery as an embolus leading to the pulmonary infarction. Pneumococci being in the blood, the pneumonic infiltration in the periphery of the infarct is easily accounted for. It is not to be forgotten, however, that there is much evidence in favor of the view that pulmonary thrombosis can occur as the result of local processes in the walls of the pulmonary artery without the occurrence of embolism. The whole subject is fully discussed in the article on thrombosis and embolism in Clifford Albutt's System of Medicine.

NOTES ON NEW BOOKS.

The Nervous System and Its Constituent Neurones. By Lewellys F. Barker, M. B., Tor., Associate Professor of Anatomy in the Johns Hopkins University; Assistant Resident Pathologist to the Johns Hopkins Hospital. (*D. Appleton & Co., New York,* 1899.)

In 1897 Dr. Barker began a series of anatomical papers in the *New York Medical Journal* for the purpose of presenting some of the most important recent discoveries relating to the nervous system. He had little idea at the commencement of his work that these papers would form a book of more than a thousand pages. For nearly two years articles on the anatomy of the nervous system appeared from Dr. Barker's pen, at irregular intervals, until the writer realized that should his method be continued, an end of his work could hardly be attained. The intense activity of investigators in this domain makes the task of keeping abreast of their discoveries a difficult one. Dr. Barker decided, therefore, that a book would be the best form in which to present the results of his labors. He accepts the neurone concept without hesitation and makes it the foundation of his work.

The book is divided into six sections, of which the last comprises much more than half of the entire volume. In these sections are considered the history of the development of the neurone concept, the external morphology of the neurones, the histogenetic relations of the neurones, the neurone as the unit in physiological and pathological processes, and the grouping and chaining together of neurones in a complex nervous system like that of man and the higher animals.

In criticizing any book it is only fair to the author that we should constantly bear in mind the object he has had before him. Dr. Barker's book is chiefly a review of the work of others, but it is a review by a man of excellent critical ability who knows how to sift the good from the bad and to present in strong light the important features of many valuable papers. It is not a book containing merely the results of Dr. Barker's original investigations, although throughout the work the author's hall-mark is found, and in many places a statement of his views on the opinions quoted from others. We find also evidences that the microscope has been diligently employed by him, and that a very large amount of literature has been carefully studied.

Dr. Barker begins his book with a brief account of the imperfect knowledge of the nervous system existing fifty or sixty years ago, and shows how, step by step, information has been gained. It is interesting to review this history. We are too prone to accept the achievements of the past without recognition of the laborious methods by which they were made possible. We find a brief account of the rise of the silver method—but not the fall, as some overzealous writers would have us believe—and the methylene-blue method of Ehrlich, that has never been so extensively employed as its value warrants, is described. Dr. Barker is one of the strongest defenders of the neurone concept. The independence of the neurone, he says, has apparently, at least so far as embryonic tissues are concerned, had its complete anatomical justification, and even granting the claims of Held, Apáthy and Bethe, the general validity of the doctrine of the individuality of the neurones would not be affected.

Van Gehuchten is said to have found changes in the terminal nucleus of a sensory nerve after sensory axones of the first order were cut—similar changes to those that occur in motor neurones. This is true, but it should be mentioned that Van Gehuchten himself later questioned the correctness of his former interpretation. The findings of Marinesco in regard to this question are said by Dr. Barker to have been curiously enough misinterpreted. Marinesco however, seems to have been correct, for Van Gehuchten has demonstrated by the silver method that the cells of the posterior nucleus of the vagus send their axis cylinders towards the periphery of the medulla oblongata, and that this posterior nucleus is motor. We need more evidence before we can accept the statement that

changes similar to those in motor cells occur in the cell bodies of the second sensory neurones after diversion of the axis cylinders of the peripheral sensory neurones.

A brief but excellent account of Apáthy's work is given. We feel that a great truth has been only partially revealed to us when we study Apáthy's writings. Whether or not Apáthy's and Bethe's statements will force us to abandon the neurone theory, the future alone can show. We must acknowledge that this concept depends on the results obtained by various methods, and that it seems impossible to explain certain findings by any other theory at present known to us; and yet the writer of this review would hardly care to say with Dr. Barker that the validity of the neurone concept has been so firmly established that it can never be utterly overthrown. The downfall of the Roman empire seemed impossible at one period, and some of the best-established theories have fallen before the revelations of science.

Dr. Barker gives Nissl's classification in as simple a form as possible. The students of medicine—for whom in part this book is written—who will carry these types in their memories do not exist in every medical school. Dr. Barker's résumé of the views held in regard to the nerve-cell is excellent. We should hardly expect that everything of importance written on this subject could be crowded into a few pages of a text-book, but the author has performed the task he set for himself; he has given a brief résumé of the work of others and an expression of opinion regarding the relative value of this work, and possibly he has given more than most students will easily grasp.

The chapters on embryology are concise and contain the most important facts. The description of the metameres is of especial value at this time, on account of the importance attributed to them in disease by certain writers. The metameres appear in the embryo as sharply defined masses in the mesoderm lateral from the chorda dorsalis and the medullary tube. A spinal nerve with its sensory and motor roots, spinal ganglion and portions of the medullary tube to which it belongs, represents a neurotome. Brissaud has recently explained many cutaneous diseases and other conditions by a theory based on the metameres. The description which Dr. Barker gives of the shifting of the diaphragm and the explanation thereby of how an abdominal muscle is supplied by a cervical nerve, are very interesting.

Dr. Barker, in his chapters on the physiology of the neurone refers to facts which are almost incomprehensible; such, for example, as the production by the activity of the neurones of chemical compounds of a degree of complexity scarcely approached elsewhere on this planet; or the preservation of memory in certain cells notwithstanding the constant changes of structure, which he expresses in the words "Dauer in Wechsel." We have in this latter statement a mystery the human mind is unable to solve. Marinesco has recently written on this subject. According to his view, the duration of a nerve-cell is as long as the duration of the organism. * * * "C'est grâce à cette fixité des cellules nerveuses que la vie psychique est possible. C'est cette propriété remarquable qui nous explique également la transmission héréditaire de certaines propriétés vitales de l'organisme. Si, en effet, les cellules nerveuses devaient sans cesse se trouver en voie de multiplication, il serait bien difficile de pouvoir expliquer la persistance remarquable de nos souvenirs, de la formation de nos idées; la transmission de l'immunité, etc." A nerve-cell may change, may grow, but there is still a "Dauer in Wechsel."

It may be permissible to correct a slight error that has crept into Dr. Barker's book. In referring to a paper by Dejerine and Spiller, Dr. Barker says that these writers contest the extension of endogenous fibers into the median triangle of Gombault and Philippe (p. 458); on the contrary, the words of Dejerine and Spiller are: "Le triangle médian de MM. Gombault et Philippe contient—à côté de fibres endogènes dont l' existence est très probable—un grand nombre de fibres exogènes ou radiculaires."

The central pathways of cranial nerves have only in slight extent been determined. This is well shown by a study of the vestibular nerve, although more knowledge has been acquired regarding the cochlear nerve. Even the most recent studies leave much to be desired. The acoustic pathway has been a favorite subject with Dr. Barker and he has written on it previously.

Dr. Barker believes that the consensus of opinion is that the function of the posterior columns of the cord is the conduction of the so-called muscular sense and not of tactile sense. In regard to tactile sense we are more uncertain. He believes that all the centripetal fibers in the inner capsule occupy the posterior part of the pars occipitalis. This view, however, is disputed by Dejerine. He agrees with Dejerine and some other investigators in teaching that most of the sensory neurones are interrupted in the optic thalamus. Little is known of the central neurones of the gustatory conduction paths, and Dr. Barker dismisses the subject in a few lines. If we compare the space allotted to the discussion of these fibers with that given to the discussion of the central olfactory tract, we realize that the latter pathway is exceedingly complex and that it is among the most difficult structures of the central nervous system to understand.

All through the book references are made to Miss Sabin's reconstructions of tracts and nuclei. This is a recent and valuable mode of studying the central nervous system, and Miss Sabin has been one of the most active workers in this field. We have an excellent proof of the value of this work in the picture of the lower olive given on page 958. A picture like this conveys a better idea of the convolutions of this body than can be obtained from a study of microscopical sections. This reconstruction demands time and care, and we read therefore with some surprise the numerous references to the extensive work Miss Sabin has accomplished.

The chapter on the central visual neurones is a very interesting one. The inaccuracy of the term "optic nerve" is pointed out, but no attempt at change—and we think the omission is wise—has been made. "Optic nerve" does not lead to the confusion that "ascending root of the fifth nerve" causes. We are somewhat surprised that the work of Vialet on the optic tracts and centers receives such scant recognition. The pupillary fibers of the optic tract and optic nerve are mentioned, but nothing is said of the extraordinary statements of Massaut concerning degeneration of these fibers.

All the important recent literature on the centers of the "upper facial" and "lower facial" nerves is not given. The investigations of Marinesco and Van Gehuchten show that the "upper facial" nucleus is a part of the pontile facial center and not a part of the oculomotor center. Marinesco has published within the past few months a second paper on this subject containing the results of his latest investigations and confirming his former statements in their most essential details.

Too much praise of the form in which this book has come from the press cannot be given. The volume is a beautiful example of the printer's art. The illustrations are numerous and well chosen. The author's style is fluent, and it is evident that Dr. Barker is a master of the English language. This book is one of which we may well be proud, and it can be said with truth that it contains the results of the most recent scientific investigations on the nervous system. We regret that the sympathetic system is passed over in silence, and express the hope that this deficiency may be remedied by the appearance of a separate monograph. W. G. S.

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